

From The Department of Clinical Neuroscience,
Division of Insurance Medicine
Karolinska Institutet, Stockholm, Sweden

SICKNESS ABSENCE - SUBSEQUENT PSYCHIATRIC MORBIDITY AND SUICIDAL BEHAVIOUR

Mo Wang



**Karolinska
Institutet**

Stockholm 2015

All previously published papers were reproduced with permission from the publisher.
Published by Karolinska Institutet. Printed by E-Print AB 2015

© Mo Wang, 2015

ISBN 978-91-7676-088-8

Sickness absence - subsequent psychiatric morbidity and suicidal behaviour

THESIS FOR DOCTORAL DEGREE (Ph.D.)

By

Mo Wang

Principal Supervisor:

Associate Professor Ellenor Mittendorfer-Rutz
Karolinska Institutet
Department of Clinical Neuroscience
Division of Insurance Medicine

Co-supervisors:

Professor Kristina Alexanderson
Karolinska Institutet
Department of Clinical Neuroscience
Division of Insurance Medicine

Professor Bo Runeson
Karolinska Institutet
Department of Clinical Neuroscience
Centre for Psychiatric Research

Opponent:

Professor Eero Lahelma
University of Helsinki
Hjelt Institute
Department of Public Health

Examination Board:

Professor Tomas Hemmingsson
Stockholm University
Centre for Social Research on Alcohol and Drugs

Associate Professor Susanna Toivanen
Stockholm University
Centre for Health Equity Studies

Professor Petter Gustavsson
Karolinska Institutet
Department of Clinical Neuroscience
Division of Psychology

“学而不思则罔，思而不学则殆。”
(孔子)

“Learning without thought is labour lost; thought without learning is perilous.”
(Confucius)

Abstract

Background: Sickness absence is a frequent recommendation in Swedish health care. Yet, research on future health outcomes of being sickness absent is sparse. Mental disorders are one of the most common diagnostic groups for sickness absence. Knowledge on psychiatric morbidity and suicidal behaviour following sickness absence is therefore of special interest. Exploring this should be done by using different sick-leave measures and by exploring differences over time, for instance, in relation to changes of social insurance regulations. The aim of this thesis was to investigate different aspects of the associations between sickness absence and subsequent morbidity, suicide attempt, and suicide.

Methods: Four population-based longitudinal cohort studies were conducted, using nationwide Swedish register data. All individuals aged 16-64 years who lived in Sweden as on 31 December 2004 (n=4 923 404), and all individuals aged 20-64 years who lived in Sweden as on 31 December 2005 or 2008 (n=4 477 678; n=4 500 400), respectively, and who were not on old-age or disability pension were followed up for six years in Study I and for two years in Study IV. In Study II, all such individuals aged 16-64 years who lived in Sweden as on 31 December 2004 and had in- or specialised outpatient care due to depressive disorders in 2005 were included (n=21 096). In Study III, 4209 individuals aged 22-65 years who committed suicide in 2007-2010 were included. In all the studies, information on socio-demographics, health care, medication, sickness absence, disability pension, and death was linked at individual level from registers held by the Social Insurance Agency, the National Board of Health and Welfare, and Statistics Sweden. Cox regression analyses were performed to estimate associations between sickness absence and inpatient care and suicidal behaviour (Study I, II, and IV). A group-based trajectory method was applied to identify sickness absence/disability pension trajectories in the five years before the suicide (Study III).

Results: Individuals who had been sickness absent, measured as incidence all-cause and diagnosis-specific sickness absence and sick-leave duration, showed a higher risk of subsequent suicide attempt and suicide compared to those without sickness absence (Study I and IV). Higher risks of suicidal behaviour associated with all-cause and diagnoses-specific sick-leave incidence and sick-leave duration were also observed among patients with depressive disorders (Study II). Among patients with depressive disorders and not on disability pension, those who had one or more incident sick-leave spells or had been full-time sickness absent had higher hazard ratios of suicide attempt in the following five years than those with no sickness absence (Study II). Individuals on sickness absence due to common mental or musculoskeletal diagnoses or with long-term sickness absence (>180 days) in 2009 had higher hazard ratios of subsequent inpatient care due to somatic disorders compared to those on such sickness absence in 2006 (i.e. before the regulatory change in 2008) (Study IV). Among those who committed suicide, five different previous sickness absence/disability pension trajectories were identified (Study III). Almost half of the suicide victims had had constantly low levels of sickness absence/disability pension, while 30% had constantly high such levels in the five years before the suicide. The trajectories were characterised by differences in socio-demographic and health care factors.

Conclusions: Sickness absence was a risk marker for suicidal behaviour, irrespective of sick-leave diagnoses, both for women and men in the general population and for patients with depressive disorders. In addition, incident mental or somatic sickness absence and long-term sickness absence after the regulatory change in 2008 might be associated with a higher medical severity than such sickness absence before the change. More knowledge is warranted on such associations as bases for preventive actions.

Svensk sammanfattning

Bakgrund: Sjukfrånvaro är en vanlig ordination inom svensk hälso- och sjukvård. Trots detta är den vetenskapliga kunskapen om samband mellan sjukfrånvaro och framtida hälsosituation synnerligen begränsad. Då den vanligaste diagnosgruppen för längre sjukskrivning är psykiska diagnoser, finns det anledning att särskilt studera samband mellan sådan sjukskrivning och senare psykiska besvär och självmordsbeteende. Studier om detta behövs där olika aspekter, inklusive sjuklighet och förändringar av socialförsäkringen beaktas, baserade på olika sjukfrånvaromått. Syftet med avhandlingen var att få ytterligare kunskap om eventuella samband mellan att vara sjukskriven och framtida sjuklighet, självmordsförsök och självmord.

Metod: Fyra populationsbaserade longitudinella kohortstudier genomfördes med hjälp av rikstäckande svenska registerdata. Alla personer som var 16-64 år gamla och som bodde i Sverige den 31/12 2004 (n=4 923 404) respektive alla personer som var 20-64 år gamla och som bodde i Sverige den 31/12 2005 eller 2008 (n=4 477 678; n=4 500 400) och som inte hade ålderspension eller sjuk- eller aktivitetsersättning följdes upp i studie I och IV. I studie II inkluderades samtliga personer som var 16-64 år gamla och bodde i Sverige 31/12 2004 och som haft slutenvård eller specialiserad öppenvård på grund av depression under år 2005 (n=21 096). I studie III inkluderades de 4209 personer, som när de var 22-65 år gamla begått självmord under 2007-2010 i Sverige. Information om sociodemografiska faktorer, hälso- och sjukvård, medicinering, sjukfrånvaro, sjuk- och aktivitetsersättning och död hämtades från registerdata från Försäkringskassan, Socialstyrelsen och Statistiska centralbyrån. Cox regressionsanalyser utfördes för att beräkna samband mellan sjukfrånvaro och slutenvård och självmordsbeteende (studie I, II, IV). I studie III användes en gruppbaserad analysmetod för att identifiera mönster av tidigare sjukfrånvaro/sjuk- och aktivitetsersättning.

Resultat: De som haft ett nytt sjukskrivningsfall, generellt respektive i specifika diagnoser samt haft längre sådana fall hade en högre risk för senare självmordsförsök respektive självmord jämfört med dem som inte hade varit sjukskrivna (studie I och IV). Motsvarande högre risk bland sjukskrivna fanns även i studien där endast patienter med depression inkluderades (studie II). Personer som varit sjukskrivna i psykiska eller muskuloskeletala diagnoser eller varit sjukskrivna >180 dagar under 2009 hade högre hazard ratio av efterföljande slutenvård på grund av somatiska sjukdomar jämfört med dem som haft motsvarande sjukfrånvaro under 2006 (dvs. före införandet av nya socialförsäkringsregler år 2008) (studie IV). Bland dem som begick självmord identifierades fem olika mönster av tidigare sjukfrånvaro/sjuk- och aktivitetsersättning (studie III). Nästan hälften av dem som begått självmord hade konstant låga nivåer av sjukfrånvaro/sjuk- och aktivitetsersättning under de fem föregående åren, medan 30 % hade haft konstant höga sådana nivåer. De olika mönstren karakteriserades av specifika sociodemografiska och sjukvårdsfaktorer.

Slutsatser: Sjukfrånvaro var en riskmarkör för senare självmordsbeteende, oberoende av sjukfrånvarodiagnos, såväl bland kvinnor som bland män. Detta gällde hela befolkningen och mer specifikt bland patienter med depression. Dessutom var incident sjukfrånvaro i psykiska och somatiska diagnoser och lång sjukfrånvaro efter införandet av nya socialförsäkringsregler associerade med senare sjukhusvistelse (och därmed ev. med mer allvarlig sjuklighet) än sjukfrånvaro innan dess införande. Mer kunskap om detta behövs för att kunna vidtaga förebyggande åtgärder.

LIST OF SCIENTIFIC PAPERS

- I. Wang M, Alexanderson K, Runeson B, Head J, Melchior M, Perski A, Mittendorfer-Rutz E. Are all-cause and diagnosis-specific sickness absence, and sick-leave duration risk indicators for suicidal behaviour? A nationwide register-based cohort study of 4.9 million inhabitants of Sweden. *Occupational and Environmental Medicine*. 2014 Jan;71(1):12-20.
- II. Wang M, Alexanderson K, Runeson B, Mittendorfer-Rutz E. Sick-leave measures, socio-demographic factors and health care as risk indicators for suicidal behavior in patients with depressive disorders - a nationwide prospective cohort study in Sweden. *Journal of Affective Disorders*. 2015 Mar 1;173:201-10.
- III. Wang M, Björkenstam C, Alexanderson K, Runeson B, Tingshög P, Mittendorfer-Rutz E. Trajectories of work-related functional impairment prior to suicide. *PloS One*. 2015 Oct 7; 10 (10): e0139937.
- IV. Wang M, Alexanderson K, Runeson B, Mittendorfer-Rutz E. Morbidity and suicidal mortality following sick leave in relation to changes of national social insurance regulations in Sweden. *Submitted*.

Contents

1	Introduction	1
1.1	Sickness absence	2
1.1.1	The Swedish sickness insurance system.....	2
1.1.2	Prevalence of sickness absence.....	3
1.1.3	Factors associated with sickness absence.....	4
1.2	Mental disorders	5
1.3	Suicide attempt and suicide	6
1.3.1	Risk factors for suicide attempt and suicide.....	9
1.4	Potential outcomes of being sickness absent.....	9
1.4.1	Sickness absence and subsequent disability pension	10
1.4.2	Sickness absence and mortality	11
1.4.3	Sickness absence and other outcomes	11
2	Aim	16
2.1	General aims.....	16
2.2	Specific aims	16
2.2.1	Study I.....	16
2.2.2	Study II	16
2.2.3	Study III.....	16
2.2.4	Study IV.....	16
3	Methods	17
3.1	Design and study population.....	17
3.2	Data sources	19
3.2.1	Longitudinal Integration Database for Health Insurance and Labour Market Studies (LISA).....	19
3.2.2	Micro Data for Analysis of the Social Insurance (MiDAS)	19
3.2.3	The National Patient Register	19
3.2.4	The Prescribed Drug Register	20
3.2.5	The Cause of Death Register	20
3.3	Exposure, covariates and outcome measures	20
3.3.1	Sickness absence and disability pension	20
3.3.2	Socio-demographic factors	22
3.3.3	Health care factors and medication.....	22
3.3.4	Suicidal behaviour.....	23
3.4	Statistical analyses.....	23
4	Results	25
4.1	Study I	25
4.2	Study II	27
4.3	Study III.....	28
4.4	Study IV.....	30
5	Discussion.....	33
5.1	Main findings	33

5.2 Discussion of results	33
5.2.1 Sick-leave diagnoses and subsequent morbidity/suicidal behaviour	33
5.2.2 Sick-leave measures and subsequent morbidity/suicidal behaviour	35
5.2.3 Trajectories of sickness absence and disability pension before suicide	36
5.2.4 Factors associated with sickness absence/disability pension and suicidal behaviour	37
5.3 Methodological considerations	38
5.4 Conclusions	40
5.5 Further research	41
6 Acknowledgements	43
7 References	45
Appendix:	
Study I-IV	

List of abbreviations

APA	American Psychiatric Association
ATC	Anatomical Therapeutic Chemical
BIC	Bayesian Information Criterion
CI	Confidence interval
CMD	Common mental disorders
DREAM	The Danish Register-based Evaluation of Marginalisation
DSM-V	Diagnostic and Statistical Manual of Mental Disorders, fifth edition
GAZEL	French Gas and Electricity Company
HR	Hazard ratio
ICD	International Classification of Diseases
IMAS	Insurance Medicine All Sweden
LISA	Longitudinal Integration Database for Health Insurance and Labour Market Studies
MiDAS	Micro Data for Analysis of the Social Insurance
PIN	Personal Identity Number
SA/DP	Sickness absence and disability pension
SAS	Statistical Analysis System
SCB	Statistics Sweden
SIA	Social Insurance Agency
SPSS	Statistical Package for the Social Sciences
WHO	World Health Organisation

1 Introduction

Sickness absence is to date a common recommendation in health care (1). In Sweden, the social insurance system provides financial compensation for lost income due to work incapacity caused by a disease or injury. In the past 20 years, concern about the occurrence of sickness absence has been expressed in several European countries as it potentially affects the sick-listed individuals and their families, employers, and the society at large (1). In Sweden, sickness absence has resulted in considerable costs for the government. In 2014, sickness benefits paid by the Swedish Social Insurance Agency (SIA) summed up to SEK 27.7 billion (2). Moreover, sickness absence may be associated with both positive and negative consequences on a person's physical, mental, and social circumstances (3). Long periods of sickness absence might not only be a marker of the severity of the disease, but might also entail social isolation and changes in health-related behaviour (alcohol and tobacco use), which might have an effect on the aggravation of symptoms (4, 5).

There has been an increasing interest in sick-leave research in recent years. Nevertheless, most of the research has mainly focused on risk factors for sickness absence, rather than on outcomes of being sickness absent (3). The following prospective cohorts are examples of projects from which data have been used in order to investigate outcomes of being sickness absent: the national gas and electricity companies (GAZEL) study in France (6), the Whitehall II study in the United Kingdom (7), the 10-Town study in Finland (8) as examples of occupational cohort studies; the Danish Register-based Evaluation of Marginalisation (DREAM) study in Denmark (9) and the Insurance Medicine All Sweden (IMAS) study in Sweden (10) as examples of population-based register studies. The mentioned occupational cohort studies are based on specific occupational groups, such as municipal workers (8, 11, 12), employees in the private/public sector (9, 13), gas/electricity workers (6, 14-18), and civil servants (7, 19). While these studies have considerable strengths through comprehensive information from questionnaires, the study populations are selected, which might restrict generalisability of findings to the general population. Sick-leave data can also be retrieved from registers of employers and of private and public insurance companies. Such register data often enable longitudinal study designs. To date, however, population-based register data are only available in few countries (20). Information on sickness absence can also be acquired by self-reported data, but shortcomings of such data include recall bias (20, 21).

Sickness absence can be measured in different ways (22-24). The number of measures used in the literature is extensive with more than 40 different measures (20, 22-24). This hampers comparison between different studies. The measures are usually constructed through three different units: sick-leave spell, time and person (20). Each of these units captures different aspects of sickness absence as a phenomenon. Based on these units, basic measures of sickness absence which are suitable for use in epidemiological studies have been previously suggested (24). Examples of these measures comprise length and duration (time based), frequency (spell based) and cumulative incidence (person based). The choice of sick-leave measures is related to the research question at hand and different measures may result in varying results. In order to give a more comprehensive view on the health conditions

investigated in epidemiological studies, the authors recommend combinations of measures related to spells, persons and time (24). As an example, sex differences were observed when using an incidence measure of psychiatric sickness absence, but not when using a time based measure (25). For these reasons, several different sick-leave measures related to the mentioned units have also been used in this thesis (see Methods).

Research on sickness absence can be categorised according to what is studied, study design, studied population, type of data and analyses, scientific discipline, perspective taken with regard to the research questions, structural level of factors included in the analyses, and type of diagnoses included (26). Table 1 shows the categorisations of studies in the current thesis, which are marked in bold.

Table 1. Categorisations of the performed studies in this thesis according to a structure for categorisations of studies on sickness absence and disability pension (26). Those relevant for the thesis are marked in bold.

What is studied	-Design -Studied -Data -Analyses	Scientific discipline	Perspective taken in research questions	Structural level of factors included in the analyses	Diagnoses
1. Factors that hinder or promote sickness absence/disability pension 3. Factors that hinder or promote return to work 2. “Consequences” of (being on) sickness absence/disability pension 4. Sickness certification practice 5. Methods, theories	<u>Study design</u> -Cross sectional <u>-Longitudinal</u> -RCT, CT, etc. <u>Studied</u> General population Insured In paid work (general or special) Diagnosed Sickness absent Other <u>Type of data</u> Interview Questionnaire Register Medical files Insurance files Notes Documents Video Other <u>Type of analyses</u> -Qualitative -Quantitative	Economy Law Management Medicine Psychology Sociology Public health Epidemiology Philosophy Other	That of the: -Society -Insurance -Healthcare -Employer -Family -Patient	-National -Local -Worksite -Health care -Family -Individual	All together Mental Musculoskeletal Cancer Circulatory Infections Other

1.1 Sickness absence

1.1.1 The Swedish sickness insurance system

The Swedish sickness insurance system regarding sickness absence covers all people above the age of 16, living in Sweden and having at least a minimum annual income from work, unemployment benefit, or parental benefit (2). The purpose of the sickness insurance system is to provide financial security in case of reduced work capacity due to a disease or injury. The compensation from the employer is referred to as sick pay, whereas compensation from Social Insurance Agency (SIA) is referred to as sickness benefit. According to the degree of

reduced work capacity, sickness benefit can be one-quarter, one-half, three-quarters, or full-term of ordinary working hours.

Sickness benefit amounts up to 80% of lost income. Employees receive sick pay from day 2-14 of a sick-leave spell from the employer (the first day being a qualifying day) (2). From day 15 employees can receive sickness benefit from SIA. A certificate from a physician is required from the eighth day of a sick-leave spell. Unemployed individuals and individuals on parental leave can be granted sickness benefit from SIA from the second day of a sick-leave spell whereas self-employed individuals receive sick pay from SIA according to which insurance coverage they have chosen.

Disability pension can be granted to all individuals aged 19-64 and living in Sweden whose work capacity has been reduced long term or permanently due to a disease or injury (2). Since 2008, temporary disability pension can only be granted to young adults aged 19 to 29 years.

In the last decade several interventions have been introduced to ensure higher quality in handling of sickness certification cases. One of these, introduced in 2007 general as well as diagnosis-specific recommendations regarding sickness certification (27-29). Previously, there was no official time limitation for how long a person could be on sickness absence with benefits. In 2008, the Swedish government launched new rules for sickness absence with the attempt to guarantee a low and stable level of sickness absence, to promote return to work earlier in the sick-leave spell, as well as to develop a standardised application of sickness insurance across the country (2, 30). Since July 2008, stricter assessments related to eligibility for sickness absence and disability pension were introduced and provision of sickness benefit for most absentees was limited to one year (2). Seriously ill people could receive sickness benefit for up to 914 days (2). In the same year, a rehabilitation chain was introduced which regulates how the reduction of work capacity should be assessed at different time points (2). Recent studies suggest that these new regulations had an impact on termination of sickness benefit and restricted transition to disability pension (27, 29, 31).

1.1.2 Prevalence of sickness absence

In most countries, sick-leave rates are rather stable over time, however, sick-leave rates have varied in some countries (1). For example, Norway had high sick-leave rates during the 1990s- and 2000s and reached a peak in 2009 (32). Denmark, on the other hand, had fairly low sick-leave rates which showed an increasing trend during the beginning of the 2000s. In Finland, relatively stable sick-leave rates were observed compared to other Nordic countries. There were fluctuations in the number of sick-leave days per sick-leave insured person in Sweden, in both women and men from 1955 to 2013 (Figure 1) (33).

Also, sex differences were observed. Since the 1980s, women have had higher number of sick-leave days than men in Sweden (Figure 1). Moreover, an increase in mental sickness absence has been observed in recent years (34). To date, mental and musculoskeletal diagnoses are the predominant sick-leave diagnoses (35, 36). The most frequent mental sick-leave diagnoses are depression, anxiety, and stress-related disorders (36).

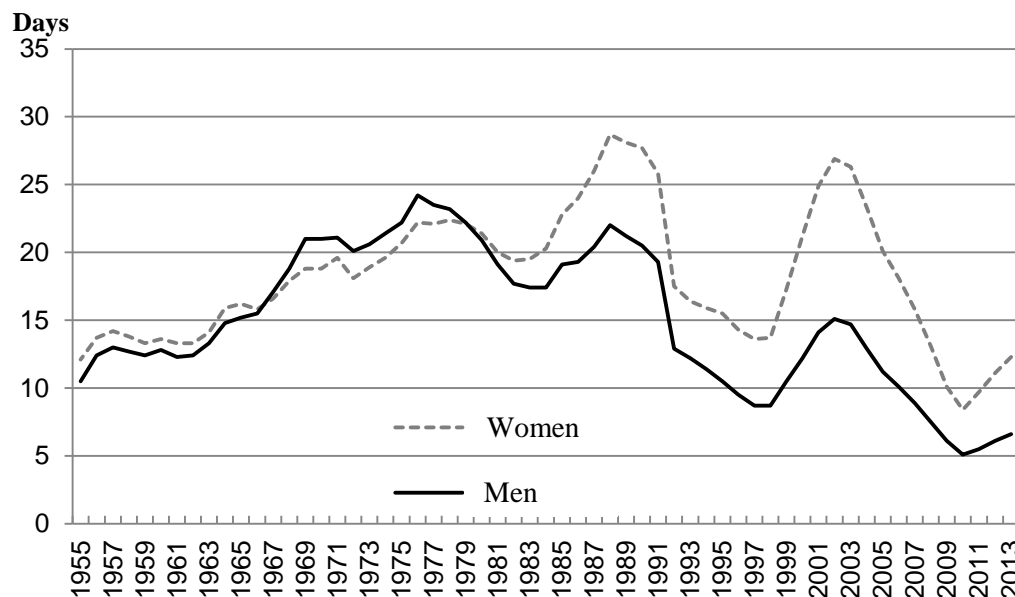


Figure 1. Number of sick-leave days with benefits from national Social Insurance Agency per sick-leave insured person, from 1955 to 2013 in Sweden (33).

1.1.3 Factors associated with sickness absence

1.1.3.1 Socio-demographic and socio-economic factors

A number of previous studies have reported associations between several socio-demographic and socio-economic factors with sickness absence (2, 35-47). In Sweden, sickness absence due to mental diagnoses is more common among women than men (2). With regard to specific mental sick-leave diagnoses, alcohol-related diagnoses have been shown to be relatively more common among men, while stress-related and anxiety diagnoses are relatively more common among women (36). The sex difference with regard to sickness absence due to musculoskeletal diagnoses is less pronounced. Concerning sickness absence due to musculoskeletal diagnoses, the most common diagnostic group is back pain, which accounted for nine percent of the sick-leave spells in 2009 among men in Sweden (women eight percent) (35). Potential sex differences may be explained by differences in morbidity, occupation, and working conditions (37-39).

Sickness absence has also been reported to be more common among older age groups (37, 40), individuals with lower educational level (40, 41), with economic difficulties (42), and with unemployment (40). Moreover, a higher prevalence of sickness absence was found in rural areas (2).

A number of studies have reported associations regarding marital status as well as having children and subsequent sickness absence (43-45, 47). Higher risk of sickness absence was found among unmarried, divorced/separated, and widows/widowers than among married people (43). Some studies reported an association between female sex and having children and risk of sickness absence (44, 47). Here, having children has been discussed as representing a double workload, which might have an impact on sickness absence (47). However, results are conflicting and other studies have shown that having multiple roles, in terms of work career and children is positive for health and work capacity (45). Additionally, migrant status appears

to be associated with a higher risk of sickness absence (46). In this thesis, a number of socio-demographic factors have been used as either exposure factors or covariates. These factors include sex, age, family situation, educational level, type of region of residence, and country of birth.

1.1.3.2 Health-related factors

Both mental and somatic complaints have been reported to predict sickness absence (48-59). Previous studies have shown associations of depressive and anxiety disorders (48-50), burnout (49, 51), and mental fatigue (49, 52) with subsequent sickness absence. Poor mental health might here be related to a job selection with poor working conditions or individuals with mental disorders might be more susceptible to psychosocial work stressors (53). Here also the possibility of reverse causality should be mentioned. This means that it is also likely that poor psychosocial working conditions are related to future mental health complaints (53).

Not only mental disorders, but also somatic symptoms such as sleep disturbance (54), physical fatigue (52, 54, 55), musculoskeletal diseases (56), and being overweight (57) have been reported to predict sickness absence. Moreover, a number of studies have shown that adverse health behaviour can be associated with future sickness absence. Focus in those studies was particularly on the association of smoking (58) and of high alcohol consumption (58, 59) with high levels of sickness absence. In this thesis, health-related factors have been primarily conceptualised as consumption of specialised health care and being prescribed specific psychiatric medication, i.e., representing a measure of the severity of the underlying disease.

1.1.3.3 Work-related factors

Work can play an important role for individuals' mental health. Besides providing a source of income, work can contribute to the structure of day and night, social contacts and a sense of meaning (60, 61). On the other hand, an adverse physical and/or psychosocial work environment can have a negative impact on mental well-being (37, 53, 61). For example, receiving social support from supervisors and colleagues has been demonstrated to be a protective factor for mental disorders such as depressive disorders (53). On the contrary, being exposed to poor working conditions or bullying are examples of risk factors for sickness absence (62-64). A number of studies have used the job demand-control-support model which was developed to measure the psychosocial working environment (65). Previous studies using this model showed that having high job demands in combination with low levels of control and support was associated with higher risk of sickness absence due to mental disorders (64, 66) and of sickness absence in general (63).

1.2 Mental disorders

Understanding the concept of mental health plays an important role for forming a comprehensive understanding of mental disorders. To date, different definitions of the concept of mental health have been put forward (67, 68). According to the definition of the World Health Organization's (WHO), mental health is "a state of well-being in which the individual realises his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community" (68).

As health in general, mental health is influenced by multiple and interacting biological, psychological, social and environmental factors (68).

On the other hand, mental disorders have been defined by the WHO as abnormal phenomena which are characterised by alterations in thinking, mood, or behaviour with personal distress and/or impaired functioning (67). Obviously, the concepts of mental health and mental disorders are not dichotomous concepts, and human behaviour lies on a continuum between mental health and mental disorders.

There are two diagnostic systems for the classification of mental disorders. One is the Diagnostic and Statistical Manual of Mental Disorders with the currently available fifth edition (DSM-V) published by the American Psychiatric Association (APA) (69). Another commonly used manual produced by the WHO is the International Classification of Diseases (ICD-10), which presents a complete list of classification of mental and behavioural disorders (70). Diagnostic information in this thesis is based on the ICD-10 codes as they build the basis for reporting diagnostic codes in the registers from the National Board of Health and Welfare and the Swedish Social Insurance Agency.

Depressive, anxiety, and stress-related disorders are often summarised as “common mental disorders” (CMD) (71). CMDs have a considerable impact on individuals’ lives through their effect on social and occupational functioning (72). Symptoms of these disorders include insomnia, fatigue, troubles in concentrating, forgetfulness, irritability, and somatic complaints (70, 73). It is common to have two or more mental disorders that occur together, which is known as comorbidity (67). Depressive disorders have, e.g., often been found to be comorbid with anxiety (74). Somatic diseases such as musculoskeletal disorders and cancer also commonly coexist with mental disorders (75-77).

Onset, prevalence, and course of mental disorders are influenced by a multiplicity of factors. Possible factors include social and economic factors, demographic factors such as sex and age, and the presence of somatic diseases (67). Anxiety and depressive disorders appear to be more common among women, while substance use disorders and antisocial personality disorders are reported to be more common among men (67). Some studies also suggest that the prescription of psychotropic medicines, including antidepressants and anxiolytics is higher among women (78). Age is another important indicator of mental disorders. Compared to many somatic disorders, mental disorders are often characterised by an early age of onset (79), which might differ between types of mental disorders (79, 80). In addition, people who are socially isolated and people who are socio-economically disadvantaged have been shown to have poorer mental health than others (67).

1.3 Suicide attempt and suicide

Suicide, an intentional self-harm resulting in death, represents a considerable public health problem since it is an important cause of mortality worldwide (81). Worldwide, up to one million individuals are estimated to commit suicide annually (82). However, suicide rates vary considerably between regions and countries. In the European region, the highest suicide rates for both males and females are found in Eastern European countries, for instance, Lithuania,

Russian Federation, and Belarus (81-83). In Sweden, the suicide rate reached a peak in the beginning of the eighties and then declined (Figure 2) (84). The decline was prominent in individuals over 24 years, whilst individuals between 15-24 years showed stable trends of suicide during the last two decades (Figure 2) (84). In 2014, the suicide rate in Sweden was 11.1 (per 100 000 inhabitants) in total, 6.1 for women and 16.2 for men (84). This was close to the average rate in the European region (82).

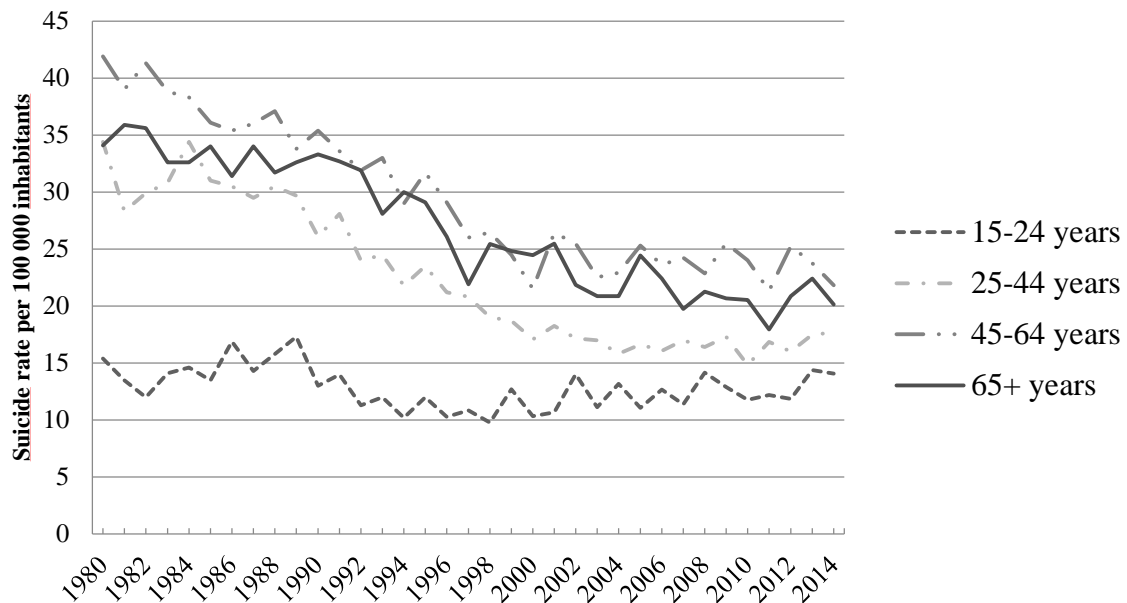


Figure 2. Suicide rate per 100 000 inhabitants in different age groups in Sweden, 1980-2014 (84).

Non-fatal intentional self-harm occurs approximately 20 times more frequently than completed suicide and is the most significant risk factor for suicide in the general population (85). Many different terms, including parasuicide, suicide attempt and deliberate self-harm have been used to describe this behaviour (85). Deliberate self-harm has been defined as an intentional self-poisoning or self-injury, regardless of the underlying motivation and of any intent to die (85-87). The term parasuicide has been described as consisting of both suicide attempts and other self-harm behaviour (85, 88). Suicide attempt has been defined as a behaviour that is self-inflicted and potentially injurious with a nonfatal outcome and that there is evidence (either explicit or implicit) showing an intent to die (85). Considering that the intent of non-fatal intentional self-harm is difficult to assess, the WHO/EURO multicenter study on suicidal behaviour has been adopting the term “suicide attempt” also in the absence of a clear suicidal intent (88). In this thesis, the term suicide attempt has been used throughout in relation to the definition by the WHO/EURO multicentre study.

Suicide attempt is often impulsive and up to one-third of the individuals surviving an attempt report not having had any suicidal intention (89). Age standardised rates of suicide attempt in the WHO/EURO study including 13 countries showed large international differences with low rates in southern European countries and high rates in northern Europe (88). In Sweden, the rate of inpatient care due to suicide attempt showed a dramatic increase among individuals aged 15-24 years during 1997 and 2007 and the rate declined after that, but

remained at a higher level than in the 1990s (90). With regard to individuals older than 24 years, relative stable trends were seen over time (See Figure 3).

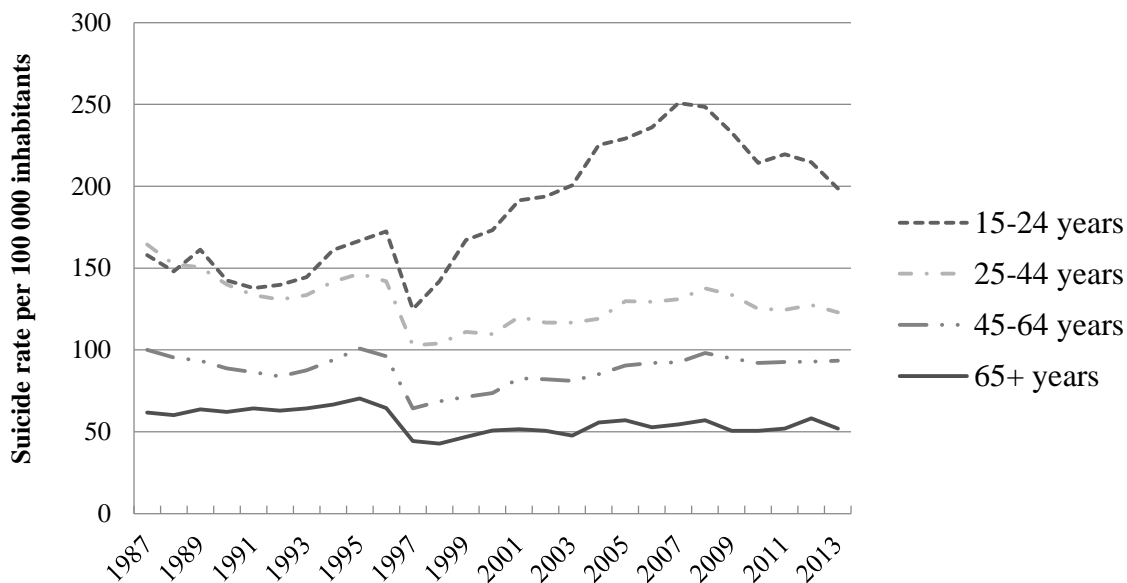


Figure 3. Suicide attempt rate per 100 000 inhabitants in inpatient care for different age groups in Sweden, 1987-2013 (90).

The choice of a specific method is an important factor in determining whether the outcome is fatal or not. Men in general tend to use more violent methods as hanging or shooting, while women more often use less violent methods as self-poisoning (83). The most common suicide method worldwide is poisoning, mainly through pesticide ingestion, especially in rural areas of many developing countries (83). In the USA, firearms are commonly used suicide methods due to their availability (83). In Sweden, poisoning is the main method of suicide among women, whereas hanging is the most commonly used method among men (84). The second most common methods for suicide in women and men are hanging and poisoning, respectively.

Suicidal behaviour (i.e., suicide attempt and suicide) as a sensitive issue is often under-reported (83). A large proportion of individuals who attempted suicide do not present to health care services (85). Previous studies showed that only approximately 25% of suicide attempters receive treatment in inpatient care (91). Even in countries with good register-based data, suicidal behaviour may be misclassified as an accident or recorded as another cause of death (81). In Sweden, the Forensic Department is responsible for conducting a forensic examination of the deceased - often with an autopsy - when the police suspects an unnatural death (84). The Forensic Department has autopsied approximately 97 percent of all suicides since 1990s. The cause of death which is reported on a death certificate is submitted to the National Board of Health and Welfare. Then, all diagnoses and injuries reported on the certificate are translated into ICD-codes. Since the introduction of the 8th revision of ICD in 1969 it is possible to classify death as an undetermined intent (84). A number of previous studies have included undetermined intent in order to limit under-reporting of suicide attempt or suicide and to account for temporal and geographical differences in ascertainment methods (92-94). This approach has also been used in this thesis.

1.3.1 Risk factors for suicide attempt and suicide

People who commit suicide have to a large extent previously attempted suicide (83). Likewise, among people who attempted suicide, a substantial share will eventually commit suicide (95). Risk factors for suicide attempt and suicide overlap to some extent (83, 85). However, some differences have also been reported. The age of first onset of suicide attempt is often during adolescence and young adulthood (96). Older people have lower risk of suicide attempt, but when they attempt suicide they might be at higher risk to commit suicide subsequently (97). Suicide, on the other hand, is more common among older people (83). While being male is a risk factor for suicide, suicide attempt occurs more often among women (83, 85). A substantial body of evidence suggests that the risk of suicidal behaviour is high in divorced, unemployed, and lower educated people and in those with low income (98-101). Moreover, studies have shown that up to 90% of people who present to hospitals because of suicide attempt or those who commit suicide fulfil the criteria of having at least one mental disorder (98, 102). Here, depressive disorders are the most common ones, followed by substance abuse and anxiety disorders (98, 102, 103). Individuals with severe mental disorders such as bipolar disorders, schizophrenia or personality disorders are also reported to have a high risk of suicide (104). Moreover, comorbidity is common (103, 105).

Individuals with depressive disorders have a many times higher risk of attempting suicide or dying due to suicide than the general population (106, 107). The life time risk of suicide for individuals who meet the criteria for a depressive disorder is around 4-15% (108-110). Individuals with depressive disorders may sometimes commit suicide during the first depressive episode, which is likely related to alcohol misuse and impulsive-aggressive personality traits (110, 111). As mentioned earlier, a history of suicide attempt has been shown to be the strongest risk factor for suicide (105, 112). Up to 40% of suicide victims have previously attempted and those with a history of suicide attempt have an up to 40 times higher suicide risk than that of the general population (83, 113). Suicide risk after suicide attempt is particularly higher among men (114), older individuals (114), individuals with repeated suicide attempts (115), those who attempt suicide with strong suicidal intent (116), individuals with alcohol abuse (117), and those living alone (117). Suicide attempt and suicide are also associated with somatic disorders, including cancer (118, 119), epilepsy (119, 120), diabetes (121), HIV/AIDS (118, 119, 122), Huntington's disease (118, 119), multiple sclerosis (118, 119) and injury (118, 119, 123). Undetected mental disorders are likely to be co-occurring with these somatic disorders (119, 124).

Moreover, results from previous studies show associations of suicidal behaviour and family history of suicide behaviour (125, 126), adverse childhood environment and experiences (93, 127), alcohol abuse (128), drug use (129), social isolation (130) and adverse life events (131). The above mentioned risk factors are often interlinked (85).

1.4 Potential outcomes of being sickness absent

Sickness absence can have an effect on the sick-listed individuals, their families, but also on employers, colleagues, social insurance systems and the society (3). In this thesis, some

possible outcomes for the individual being on sickness absence have been studied. Potential outcomes of being sickness absent can involve different types of consequences on well-being, working life, economy, social life and lifestyles etc. (3). Potential positive and negative outcomes of being sickness absent regarding different dimensions are described below (Table 2) (3).

Table 2. Summary of potential outcomes of being sickness absent regarding different aspects (3).

Health	Health, e.g., in terms of well-being, ability to take action, sense of meaning, or quality of life may improve or become worse following a sick-leave spell.
Work capacity	Work capacity may improve or decline as an outcome of sickness absence.
Disease	The disease causing sickness absence may improve or become worse during the sick-leave spell. Other diseases may develop during the sickness absence, e.g., depression.
Sickness absence	Sickness absence may lead to prolonged or future sickness absence.
Disability pension	Sickness absence may lead to disability pension.
Premature death	Sickness absence may increase the risk for premature death.
Working life	Sickness absence may be a risk for full or partial unemployment. Work conditions and work tasks can be changed in positive or negative ways. Career opportunities and personal finances may be influenced.
Social life	Social contacts and activities may be influenced in positive or negative ways.
Life style	Exercise, diet, tobacco use, alcohol use, drug use, and risk behaviours (e.g., suicide attempt) may be changed in positive or negative ways.
Emotional aspects	Life satisfaction, self-confidence, self-image, and self-awareness may be altered in positive or negative ways. Stress and boredom may appear due to sickness absence.

In order to review studies on potential outcomes of being sickness absent, a literature search via PubMed was conducted in May 2015 for studies published in scientific journals during 2000 to 2015. The following search terms were used: sickness absence, sick leave, health outcome, social outcome, disability pension, mortality, suicide attempt, suicide, or recurrence based on the search terms used in a systematic review published in 2004 (3). The predominant number of the identified studies regarding subsequent outcomes of being sickness absent has focused on either disability pension or mortality as possible outcomes. Some other studies focused on subsequent health conditions, future sickness absence, work capacity, and life situation.

1.4.1 Sickness absence and subsequent disability pension

Several prospective cohort studies have reported a positive association between all-cause or diagnosis-specific sickness absence and subsequent disability pension (8, 9, 17, 132-147). The main findings from these studies were that long-term or increasing duration of sickness absence were associated with higher risks for being granted disability pension compared to those not being sickness absent (8, 17, 135, 146). Sickness absence with the following sick-leave diagnoses have been investigated: mental (17, 132, 137-140), musculoskeletal (17, 134, 138), circulatory (17, 132), nervous (132), respiratory (17, 132), and otoaudiological diagnoses (141). Also, two studies reported an association between partial sickness absence and subsequent partial disability pension (142, 143).

1.4.2 Sickness absence and mortality

Associations between sickness absence and mortality have been studied in several European countries (Table 3). Among these studies, all-cause sickness absence, several sick-leave spells, and long sick-leave duration have been shown to be associated with higher risks of all-cause mortality (7, 11, 13, 19, 148-150). Moreover, sickness absence has also been reported to be predictive of mortality due to cardiovascular diseases, cancer, and suicide (7, 11, 151, 152). Several studies have investigated specific sick-leave diagnoses and mortality, showing that sickness absence due to mental, musculoskeletal, circulatory, cancer, respiratory, digestive, and neurological diagnoses was associated with higher risk of subsequent premature death (6, 7, 10, 15, 148, 152, 153).

To date, a limited number of studies have reported association between sickness absence and suicide (10, 11, 15, 125, 149, 152-155). All-cause sickness absence has been found to be a risk indicator of suicide in a large prospective cohort study in Finland (11). Two Danish studies reported a similar association (125, 154). Moreover, in an occupational cohort study of employees of the French Gas and Electricity Company (GAZEL), mental sickness absence was a strong risk indicator of suicide (15). Also, a number of Swedish cohort studies reported a higher risk of suicide among people with increasing number of sick-leave days, sickness absence due to specific mental diagnoses, and due to musculoskeletal diagnoses (10, 149, 152, 153, 155). Table 3 provides more detailed information on study design of the studies on sickness absence and subsequent mortality.

1.4.3 Sickness absence and other outcomes

Some previous studies have also focused on the association of sickness absence with outcomes such as sub-optimal health and mental disorders, measured in different ways (Table 4). In a prospective study of the French GAZEL cohort, sickness absence was reported to be associated with subsequent depression (14). Compared with employees with no sickness absence during the study period, those with sickness absence were more likely to be depressed, after adjustment for socio-demographic and health-related factors. Both mental and somatic sickness absence were risk indicators of future depression.

Moreover, sickness absence has been reported to be a risk indicator of future sub-optimal health (16, 18, 156, 157). Long-term sickness absence as well as sickness absence due to specific mental and somatic diagnoses were associated with subsequent sub-optimal health (16). Another prospective occupational cohort study showed similar associations, which differed by occupational positions (18). In addition, sickness absence has been observed to be a risk indicator of future sickness absence (12, 52, 158-160) (Table 4). Sickness absence has also been related to a number of subsequent adverse social situations: job termination and unemployment (161, 162), worse financial situation (163), or social exclusion (5)

Table 3. Summary of studies on sickness absence and subsequent mortality (studies with suicide as outcome are indicated in bold).

Author, year published, country	Study design; Type of data	Study period	Exposure	Outcome measures	No. in study population	Covariates	Results
Qin et al. 2000 (154), Denmark	Prospective population based case-control study; Register	1980-1994	Sickness absence >3 weeks	Suicide	811 suicide cases, 79 871 controls	Socio-demographic and socio-economic factors, disability pension, mental disorders, and drug use	Sickness absence is associated with suicide in men.
Qin et al. 2003 (125), Denmark	Retrospective population based case control study; Register	1981-1997	Sickness absence >3 weeks	Suicide	21 169 suicide cases, 423 128 controls	Socio-demographic and socio-economic factors, disability pension, and mental disorders	Sickness absence is associated with suicide in both men and women.
Kivimäki et al. 2003 (19), UK	Prospective occupational cohort study; Register, company records, survey	1985-1998	Sickness absence < and >7 days	All-cause mortality	10 308 civil servants	Age, employment grade, common clinical conditions, self-rated health, and chronic illness	More sick-leave spells are associated with all-cause mortality. Sickness absence <7 days seems to be protective.
Vahtera et al. 2004 (11), Finland	Prospective occupational cohort study; Register, company records	1990-2001	Sickness absence < and >3 days	All-cause and cause-specific mortality	41 736 full time municipal employees	Age, employment grade, and type of employment	More than one spell is associated with all-cause and cause-specific mortality (Suicide, circulatory, cancer, alcohol related).
Gjesdal et al. 2008 (148), Norway	Prospective population-based cohort study; Register	1994-2003	Sickness absence >8 weeks, diagnosis-specific sickness absence	All-cause mortality	3386 persons with sickness absence compared to 256 654 inhabitants	Age, income	All cause and cause-specific sickness absence are associated with all-cause mortality.
Head et al. 2008 (7), UK	Prospective occupational cohort study; Register, company records, survey	1985-2004	Sickness absence >7 days, diagnosis-specific sickness absence	All cause and cause-specific mortality	6478 civil servants	Age, sex, and employment grade	Information on diagnoses of sickness absence improves prediction of mortality.
Kivimäki et al. 2008 (151), France	Prospective occupational cohort study; Company records, survey	1990-1992	Sickness absence >28 days	All cause mortality	17 948 employees in GAZEL	Age, sex, socio-economic status, and comorbidity	High number of sick-leave days and spells is associated with mortality.
Singh-Manoux et al. 2008 (150), UK and France	Prospective occupational cohort study; Register, company records, survey	1985-2004 1989-2005	Sickness absence ≥15 days	All cause morbidity and mortality	10 308 civil servants in Whitehall II, 20 625 employees in GAZEL	Age, employment grade, and marital status	Sickness absence is associated with mortality among men in the Whitehall II cohort.

Table 3. (Continued)

Author, year published, country	Study design; Type of data	Study period	Exposure	Outcome measures	No. in study population	Covariates	Results
Ferrie et al. 2009 (6), France	Prospective occupational cohort study; Company records	1990-2007	Sickness absence >7 days, diagnosis-specific sickness absence	All-cause mortality	19 235 employees in GAZEL	Age, employment grade	All-cause and diagnosis-specific sickness absence are associated with all-cause mortality.
Lund et al. 2009 (13), Denmark	Prospective population-based cohort study; Register	2001-2004	Sickness absence 1-53 weeks	All-cause mortality	236 107 employees in private sector	Age, sex, and employment grade	Mortality increases with increasing duration in sickness absence. There are differences in sex and occupational grade.
Melchior et al 2010 (15), France	Prospective occupational cohort study; Register, company records	1990-2008	Sickness absence >7 days, diagnosis-specific sickness absence	Cause-specific mortality	19 962 employees in GAZEL	Age, sex, employment grade, marital status, smoking, and alcohol use	Sickness absence due to mental diagnoses is associated with suicide.
Jansson et al. 2012 (152), Sweden	Prospective population-based cohort study; Register	2005-2009	Sickness absence due to musculoskeletal diagnoses	All-cause and cause-specific mortality	4 760 987 individuals	Socio-demographics, in- and specialised outpatient care	Sickness absence due to musculoskeletal diagnoses is associated with all-cause mortality and mortality due to cancer, circulatory diseases, mental disorders, and suicide.
Mittendorfer-Rutz et al. 2012 (10), Sweden	Prospective population-based cohort study; Register	2004-2008	Sickness absence due to mental diagnoses	All-cause and cause-specific mortality	4 857 943 individuals	Socio-demographics, in- and specialised outpatient care	Mental sickness absence is associated with all-cause mortality and mortality due to suicide, cancer, and circulatory diseases.
Bryngelson et al. 2013 (153), Sweden	Prospective occupational cohort study; Register	1990-2007	Sickness absence >90 days due to mental diagnoses	All-cause and cause-specific mortality	244 990 employees within municipalities and counties in 1990 and 764 137 in 2000	Socio-demographics, inpatient care	Long-term mental sickness absence is associated with all-cause mortality and mortality due to suicide.
Lemogne et al. 2013 (155), France	Prospective occupational cohort study; Register, company records, survey	1989-2010	Sickness absence due to mental diagnoses	Cause specific mortality	20 625 employees in GAZEL.	Age, sex, employment grade, alcohol use, smoking, height, and weight	Mental sickness absence is associated with cardiovascular mortality and non-cardiovascular mortality.
Björkenstam et al. 2014 (149), Sweden	Prospective population-based cohort study; Register	1994-2006	All-cause sickness absence, sick-leave days	All-cause and cause-specific mortality	4 669 235 individuals	Socio-demographics and inpatient care	Higher number of sick-leave days is associated with all-cause mortality and mortality due to circulatory disease, cancer, and suicide.

Table 4. Summary of studies on sickness absence and subsequent sub-optimal health, future sickness absence and adverse mental health outcomes

Author, year published, country	Study design; Type of data	Study period	Exposure	Outcome measures	No. in study population	Covariates	Results
Kivimäki et al. 2008 (157). UK	Prospective occupational cohort study; Company records, survey	1985-1993	Sickness absence >7 days	Health status	5210 civil servants	Age, sex, baseline health measures, employment grade, health-related risk factors, and psychosocial factors	Low sick-leave rates are associated with positive change in health status among employees with poor health.
Melchior et al. 2009 (14), France	Prospective occupational cohort study; Company records, survey	1996-1999	Sickness absence >7 days, diagnosis-specific sickness absence	Depression	7391 employees in GAZEL	Age, sex, marital status, employment grade, smoking, alcohol use, depressive symptoms, and work stress	Mental and non-mental sickness absence predicts future depression.
Roelen et al. 2010 (159), Netherlands	Prospective occupational cohort study; Company records	2001-2007	Diagnosis-specific sickness absence	Incidence of recurrent sickness absence after return to work	137 172 employees in Dutch Post and Telecom	Sex, age, salary scales, socio-economic status, marital status, and type of employment	Sickness absence due to musculoskeletal diagnoses has highest recurrence, followed by mental diagnoses.
Vahtera et al. 2010 (16), France	Prospective occupational cohort study; Company records, survey	1990-2006	Sick-leave days and diagnosis-specific sickness absence	Self-rated health	15 320 employees in GAZEL	Sex, age, employment grade, and the year of retirement	Employees with 30 absence days have higher risk for suboptimal health. Sick-leave diagnoses are associated with sustained suboptimal health.
Ferrie et al. 2011 (18), France	Prospective occupational cohort study; Company records, survey	1990-2006	Sick-leave days and diagnosis-specific sickness absence	Sub-optimal health	15 320 employees in GAZEL	Sex, age, and chronic illness	Sickness absence of more than 30 days is associated with future sub-optimal health in all occupational positions.
Gustafsson et al. 2011 (156), Sweden	Prospective cohort study; Register, survey	2004-2006	Sickness presence and sickness absence	Health problems and work capacity	2181 employees	Sex, age, education, socio-economic status, work-related factors	Sickness presence and sickness absence are predictors of future poor health, physical complaints, low mental well-being and low work capacity.
Koopmans et al. 2011 (158), Netherlands	Prospective occupational cohort study; Company records	2001-2007	Sickness absence due to common mental disorders (CMDs)	Recurrent sickness absence after return to work	9904 employees in Dutch Post and Telecom	Sex, age, marital status, duration of employment, type of employment, and company	Employees with a previous episode of sickness absence with CMDs are at higher risk of recurrent sickness absence with CMDs.

Table 4. (Continued)

Author, year published, country	Study design; Type of data	Study period	Exposure	Outcome measures	No. in study population	Covariates	Results
Roelen et al. 2011 (160), Netherlands	Prospective occupational cohort study; Company records	2004-2008	Sick-leave spells and durations	Future sickness absence	551 employees in a hospital	Age and sex	Sick-leave days and episodes are associated with risk of future sickness absence.
Laaksonen et al. 2013 (12), Finland	Prospective occupational cohort study; Company records, survey	2000-2007	Sick-leave spells and durations	Future sickness absence	6934 municipal employees	Employment grade, working conditions and health-related behaviours	Preceding sickness absence is associated with risk of new sick-leave episodes. The association is stronger for longer sick-leave spells and for men.
Roelen et al. 2013 (52), Norway	Prospective occupational cohort study; Survey	2008-2010	Sick-leave durations	Future sickness absence	2059 nurses	Individual, private life, and work variables	Number of sick-leave days predicts future sickness absence.

2 Aim

2.1 General aims

The general objective of this thesis was to investigate different aspects of the association between sickness absence and subsequent morbidity, suicide attempt and suicide, when simultaneously taking socio-demographics, previous and current morbidity and medication into consideration.

2.2 Specific aims

2.2.1 Study I

The aim of the first study was to investigate all-cause and diagnosis-specific sickness absence as well as sick-leave duration as risk indicators for suicide attempt and suicide among women and men.

2.2.2 Study II

The second study aimed to examine whether sickness absence measured in different ways (regarding length, grade (full- or part- time), diagnoses, and number of spells), socio-demographics, medication, and health care predict suicide attempt and suicide among patients with depressive disorders from in- or specialised outpatient health care.

2.2.3 Study III

The aim of the third study was to identify trajectories of sickness absence and disability pension prior to suicide and to describe associations of socio-demographic and health care factors with such trajectories.

2.2.4 Study IV

The aim of the fourth study was to 1) scrutinise the association between all-cause and diagnosis-specific sickness absence and sick-leave duration with subsequent risk of inpatient care due to mental and somatic disorders, as well as suicide attempt and suicide, and 2) analyse possible differences in socio-demographics and previous and current morbidity-related measures in individuals on sickness absence before and after the changes in the social insurance regulations in 2008 in Sweden.

3 Methods

The design and methods applied in each study are summarised in Table 5.

3.1 Design and study population

Population-based prospective/retrospective cohort design was applied in the four studies in the thesis.

In Study I, 4 923 404 individuals who lived in Sweden on 31 December 2004, aged 16-64 years, without old-age or disability pension during 2005 and with no ongoing sick-leave spell at the turn of 2004/2005 were included. Individuals with old-age or disability pension were considered not to be under risk of being sickness absent and therefore they were not included. By excluding sick-leave spells at the turn of 2004/2005, an investigation of incident sickness absence was enabled. The final cohort was followed up from 1 January 2005 for six years through 31 December 2010, with respect to suicide attempt and suicide.

In Study II, the study population comprised all individuals, aged 16-64 years and living in Sweden on 31 December 2004, not on old-age or disability pension throughout 2005, who had in- or specialised outpatient health care due to depressive disorders in 2005. In- or specialised outpatient health care due to depressive disorders was defined according to the ICD-10 codes F32 (depressive episode) or F33 (recurrent depressive disorder). Among individuals hereby identified, those who between 2000 and 2005 also had had an in- or specialised outpatient care due to schizophrenia (ICD-10 code F20-29) or bipolar disorder (F31), were excluded. Thus, 21 096 individuals were included in the study and they were followed up from 1 January 2006 through 31 December 2010, with respect to suicide attempt and suicide.

In Study III, the study population included all individuals who committed suicide during 2007-2010 when aged 22-65 years (n=4209). Suicide was defined according to the ICD-10 codes X60-X84 and Y10-Y34 (event of undetermined intent), as suicide is often under-reported or recorded as undetermined intent (92-94). An annual time-scale was applied where time point T-5 represented 5 years prior to suicide (i.e. 2002-2005). The time during T-5 to T-1 (i.e., 2002-2009) was used to investigate how trajectories of sickness absence and disability pension developed over the five years prior to suicide.

In Study IV, there were 4 477 678 individuals alive, resident in Sweden, aged between 20 and 64 years on 31 December 2005 included at baseline. An additional cohort comprised individuals alive, resident in Sweden, aged between 20 and 64 years on 31 December 2008 (n=4 500 400) at baseline. Individuals with old-age or disability pension during 2006/2009 in the respective cohort as well as individuals with ongoing sick-leave spell at the turn of 2005/2006 and 2008/2009 in the respective cohort were excluded. The two cohorts were followed up for two years (2007-2008 and 2010-2011, respectively) with respect to inpatient care and suicidal behaviour.

Table 5. Overview of the four studies.

	Study I	Study II	Study III	Study IV
Aim	To examine associations between sickness absence in general, different diagnoses of sickness absence, sick-leave duration with subsequent suicide attempt and suicide	To examine whether measures of sickness absence in different ways, socio-demographics, medication, and health care were associated with subsequent suicide attempt and suicide among patients with depressive disorders	To identify trajectories of sickness absence and disability pension five years before suicide and to describe associations of socio-demographic and health care factors with sickness absence and disability pension trajectories	To investigate cohort differences and associations between all-cause, diagnosis-specific sickness absence and sick-leave duration with subsequent inpatient health care and suicidal behaviour before and after the social insurance regulatory change in 2008
Design	Prospective cohort study with baseline data on 31 December 2004 and follow-up until 31 December 2010	Prospective cohort study with baseline data on 31 December 2004 and follow-up until 31 December 2010	Retrospective cohort study with baseline data regarding inclusion in 2007-2010. Retrospective data from 2002-2005	Prospective cohort study with baseline data on 31 December 2005 (Cohort 2006) and 31 December 2008 (Cohort 2009), and follow-up until 31 December 2008 (Cohort 2006) and until 31 December 2011 (Cohort 2009)
Study population; n	4 923 404 (47.5% women; aged 16-64 at baseline)	21 096 (59.9% women; aged 16-64 at baseline)	4209 (29.1% women; aged 17-61 at baseline)	4 477 678 (Cohort 2006, 47.4% women) and 4 500 400 (Cohort 2009, 47.7% women) both aged 20-64 at baseline
Inclusion criteria	On 31 December 2004: alive, living in Sweden, aged 16-64, not on old age pension or disability pension during 2005, not on ongoing sick-leave spell at the turn of 2004/2005	On 31 December 2004: alive, living in Sweden, aged 16-64, not on old age pension or disability pension during 2005, had in- or specialised outpatient health care due to depressive disorders in 2005	In 2007-2010: had committed suicide when aged 22-65	On 31 December 2005 or 31 December 2008: alive, living in Sweden, aged 20-64, not on old age pension or disability pension during 2006/2009, not on ongoing sick-leave spell at the turn of 2005/2006 and 2008/2009, respectively
Data sources	LISA ¹ , MiDAS ² , National Patient Register, Prescribed Drug Register, Cause of Death Register	LISA ¹ , MiDAS ² , National Patient Register, Prescribed Drug Register, Cause of Death Register	LISA ¹ , National Patient Register, Cause of Death Register	LISA ¹ , MiDAS ² , National Patient Register, Prescribed Drug Register, Cause of Death Register
Outcome measures	Suicide attempt (n=17 693) and suicide (n=3356)	Suicide attempt (n=1 209) and suicide (n=152)	Trajectories of sickness absence and disability pension months	Mental inpatient care (Cohort 2006: n=30 986; Cohort 2009: n=34 843), somatic inpatient care (Cohort 2006: n=536 404; Cohort 2009: n=559 090), suicide attempt (Cohort 2006: n=3350; Cohort 2009: n=3579) and suicide (Cohort 2006: n=1821; Cohort 2009: n=1232).
Factors included in the analyses	Sex, age, educational level, type of region of residence, country of birth, family situation, previous suicide attempt, previous in- and specialised outpatient mental health care and current antidepressants	Sex, age, educational level, type of region of residence, country of birth, family situation, previous suicide attempt, previous and ongoing inpatient mental and somatic health care and current antidepressants and anxiolytics	Sex, age, educational level, type of region of residence, country of birth, family situation, suicide attempt, in- and specialised outpatient mental and somatic health care	Sex, age, education, type of region of residence, country of birth, family situation, previous suicide attempt, previous and ongoing in- and specialised outpatient mental and somatic health care and current antidepressants
Statistical analyses	Descriptive Cox proportional hazards regression models	Descriptive Cox proportional hazards regression models	Descriptive Group-based trajectory modelling Multinomial logistic regression Chi ² -test	Descriptive Cox proportional hazards regression models

¹LISA: Longitudinal Integration Database for Health Insurance and Labour Market Studies;²MiDAS: Micro Data for Analysis of the Social Insurance.

3.2 Data sources

The studies in the thesis were based on the Insurance Medicine All Sweden (IMAS) project (10), including de-identified annual register data obtained from nationwide registers from Statistics Sweden (SCB), the National Board of Health and Welfare, and the Social Insurance Agency (SIA). The personal identity numbers (PIN) attributed to all Swedish inhabitants were used to link information from the different registers (164).

3.2.1 Longitudinal Integration Database for Health Insurance and Labour Market Studies (LISA)

The Longitudinal Integration Database for Health Insurance and Labour Market Studies (LISA) was established in 1990 and is updated annually by SCB (165). LISA includes all individuals aged 16 years and older who were registered as living in Sweden on 31 December for the here studied years (165). The database contains information on social-demographics and social insurance measures (165). LISA data was used in Study I, II, and IV to define the respective study population. LISA was also used in all the four studies to obtain information on socio-demographic factors at baseline, including sex, age, educational level, country of birth, type of region of residence, and family situation. In Study III, information on sickness absence and disability pension during 2002-2009 was obtained from LISA. In Study I, II, and IV information on emigration from LISA was used for censoring in the calculation of the follow-up time.

3.2.2 Micro Data for Analysis of the Social Insurance (MiDAS)

The database called Micro Data for Analysis of the Social Insurance (MiDAS) includes annual data from SIA, from the year 1994 and onwards, covering detailed information on sickness benefits and disability pension (166). In Study I, II, and IV, MiDAS data on sickness absence regarding start date, sick-leave diagnoses and duration/length, number of sick-leave spells and sick-leave grade (i.e. full- or part-time) have been used. The register includes information on the main sick-leave diagnoses since 2005, using ICD-10 codes. Moreover, information on disability pension during exposure time was used to exclude individuals from the study population in Study I, II, and IV.

3.2.3 The National Patient Register

The National Patient Register from the National Board of Health and Welfare includes information on inpatient care and specialised outpatient care and was established in 1964, when data on inpatient care due to somatic disorders was started to be collected in six Swedish counties (167). In 1973, register data on mental inpatient care was started to be collected. Since 2001, it is compulsory to report specialised outpatient visits (167). Coverage of the inpatient care register is almost 100% (167). The National Patient Register does not include information from primary health care. In all four studies, the National Patient Register was used to obtain data on mental and somatic in- and specialised outpatient care, and suicide attempt from inpatient care. In Study II, information on depressive disorders from in- and specialised outpatient care was obtained from the National Patient Register to identify the study population.

3.2.4 The Prescribed Drug Register

The Prescribed Drug Register, held by the National Board of Health and Welfare, was established in July, 2005 (168). The register includes information with personal identity number (PIN) for all dispensed prescribed drugs in Sweden (168). The database contains information on patients and prescribed drugs (e.g., dispensed item, dosage, amount, and date) (168). All drugs are categorised according to the Anatomical Therapeutic Chemical (ATC) classification system (169). Information on antidepressants and anxiolytics from the Prescribed Drug Register was used in Study I, II, and IV.

3.2.5 The Cause of Death Register

The Cause of Death Register is held by the National Board of Health and Welfare. The register was established in 1952, aiming to record all deceased individuals, regardless of whether the death occurred in Sweden or abroad (84). The causes of death are for the years studied classified according to ICD-10 (84). In Study I, II, and IV, the Cause of Death Register was used to identify the outcome, suicide deaths. In Study III, the register was used to identify the study population (completed suicide). The register was also applied to exclude individuals who died during the exposure time in Study II and IV. In Study I, II, and IV, information on death was also used for censoring in the calculation of the person time.

3.3 Exposure, covariates and outcome measures

The exposure, covariates, and outcome measures included in the four studies are described below. All socio-demographic, health care and medication factors in Study I, II, and IV were measured either before exposure, before and during the years of exposure, or during the years of exposure. In Study III, these factors were measured at a time point five years before suicide (T-5).

3.3.1 Sickness absence and disability pension

In Study I, II, and IV, sickness absence was used as the exposure and measured in different ways, considering the number of spells, the extent (grade), the time (duration and length), as well as diagnoses.

3.3.1.1 Spells

With regard to information on spells, the focus in Study I, II, and IV was on: a) first new (incident) sick-leave spell initiated in 2005 (Study I), 2006 (Study IV), and 2009 (Study IV); b) all new (incident) sick-leave spells initiated in 2005 (Study II), and c) ongoing (prevalent) sick-leave spells in 2005 (baseline) and the year before baseline (Study II). In Study II, the number of all new sick-leave spells initiated during 2005 was measured and grouped as 1 or more than 1 spells. Individuals with no incident or prevalent sick-leave spell during the respective exposure year were used as the reference group in Study I, II, and IV.

3.3.1.2 Grade

Moreover, sick-leave grade was considered in Study II and measured by full-time and part-time sickness absence and classified as either having full-time sickness absence throughout in

all new sick-leave spells during 2005, or as having at least some part-time (<100%) sickness absence in any new sick-leave spell during 2005.

3.3.1.3 Duration and length

With regard to the time on sickness absence, both duration of the first incident sick-leave spell and length when combining sick-leave days from several spells, were used. Sick-leave duration comprises the number of sick-leave days in the first new spell initiated during the year of exposure, while sick-leave length was defined as the sum of sick-leave days in all new spells initiated during the exposure period (24). In Study I and IV, sick-leave duration was defined as the number of gross days and grouped into five categories: 1-14, 15-90, 91-180, 181-365, and more than 365 days. That is, the sick-leave spell was followed until the end, even if that extended into subsequent years. In Study II, sick-leave length, namely the total number of gross days was measured and categorised in 1-90, 91-365, and more than 365 days. Here, fewer categories of sick-leave length were used due to the fewer cases of suicidal behaviour.

3.3.1.4 Diagnoses

With regard to diagnoses of sick-leave spells, both all-cause and diagnosis-specific sickness absence were used (Study I, II, and IV). Diagnoses of sickness absence were classified according to ICD-10. In Study I, sick-leave diagnoses of the first new sick-leave spell in 2005 were categorised into 20 groups: as mental and behavioural disorders (F00-F99), and specific somatic diagnoses, i.e. all remaining 19 chapters of the ICD-10. Sick-leave diagnoses which were associated with less than 20 cases of suicide attempt/suicide and those with missing diagnoses (20%) were combined into other disorders in the analyses.

In Study II, the sick-leave diagnoses of the new sick-leave spells initiated during 2005 were categorised as at least one new sick-leave spell with a mental diagnosis (F00–F99), as having somatic sick-leave diagnoses (all other ICD-10 codes), or as missing information on diagnoses (1.6%). In Study IV, sick-leave diagnoses of the first new sick-leave spell in 2006/2009 were classified into: common mental disorders (CMD) which included “depressive disorders” (F32-F33), “anxiety disorders” (F40-42), and “stress-related disorders” (F43); all other mental diagnoses (F00-F31, F34-F39, F44-F99); musculoskeletal diagnoses (M00-99) and other somatic (other than musculoskeletal) diagnoses. Missing diagnoses (≈13%) were categorised as an own group.

3.3.1.5 Sickness absence/disability pension

In Study III, a combined measure of days with sickness absence and disability pension was used as a measure of work incapacity. Prevalent sickness absence and disability pension days during a year were combined and calculated as the mean annual number of sickness absence and disability pension net days from the time period five years before the suicide (T-5) to the time period of one year prior to suicide (T-1; i.e. 2006-2009) in order to measure work incapacity. The number of net days was thereafter transformed to the number of annual months with sickness absence and disability pension.

3.3.2 Socio-demographic factors

Socio-demographic factors at baseline were used either as covariates (Study I, II, and IV) or as exposure factors (Study II and III). These factors included information on sex, age, educational level, type of region of residence, country of birth, and family situation. Information on labour market status was included in Study II. In Study I, all analyses were stratified by sex.

In Study II, sub-groups of classification of socio-demographic factors which were hypothesised to be associated with lower risks compared to other groups in relation to suicidal behaviour were used as reference groups. In Study I and II, age was classified as 16-24 (reference group in Study I), 25-34, 35-44 (reference group in Study II), 45-54, 55-64 years. In Study III, age groups were divided into 17-27 (reference group), 28-38, 39-49, 50-61 years. In Study IV, age was classified as 20-24 (reference group), 25-34, 35-44, 45-54, 55-64 years. Educational level was grouped as compulsory (≤ 9 years), high school (10-12 years) and university (>12 years) (reference group in Study I-IV) in all the studies. Labour market status was classified into two groups in Study II: employed/self-employed (reference group) and unemployed. Type of region of residence was measured according to the number of inhabitants in a specified area (170) and categorised as big cities (reference group in all the studies), medium sized cities, and small towns/villages in all the studies.

In Study I, III, and IV, country of birth was categorised into Sweden (reference group in all the studies), other Nordic countries, EU 25 without Nordic countries, and the rest of the world. In Study II, the categories “other Nordic countries” and “EU 25” were combined due to fewer cases of outcome. The variable family situation was based on two variables in the LISA dataset: family position and family type. In Study I, III, and IV, family situation was classified into married/living with partner without children (reference group in all the studies), married/living with partner with children, single/divorced/separated/widowed without children, single/divorced/separated/ widowed with children, and adolescents living with parents, 16-20 years. In Study II, the category “adolescents living with parents” was combined with single living without children due to few outcome cases.

3.3.3 Health care factors and medication

Information on in- and specialised outpatient care due to mental and somatic disorders was used as covariates (Study I, II, and IV), exposure measures (Study II and III) or outcome measures (Study IV). As a covariate and exposure variable, previous and/or ongoing in- and specialised outpatient care due to mental (ICD-10:F00-F99) or somatic (other ICD-10 codes) disorders was categorised based on the median length of inpatient care and median number of outpatient care visits during a defined period of time. When health care was treated as an outcome, presence or absence of such care was dichotomised.

Information on antidepressant and/or anxiolytic prescription was used as covariates (Study I, II, and IV) or exposure (Study II). It was coded following the ATC codes, namely N06A and N05B. Information on antidepressant and anxiolytic prescription was used as a proxy of medical severity of underlying mental disorders. In Study I and IV, antidepressants were

included in the analyses as a dichotomised variable. In Study II, antidepressants and anxiolytics were categorised as no antidepressants and anxiolytics, only antidepressants, only anxiolytics and both antidepressants and anxiolytics.

3.3.4 Suicidal behaviour

In this thesis, suicide attempt was not only used as a measure of exposure/covariate (Study I-IV), but also an outcome measure (Study I, II, and IV). Suicide attempt was measured according to ICD-10 codes X60-X84 (intentional self-harm) in Study I and II, while an approach of combining ICD-10 codes X60-X84 and Y10-Y34 (event of undetermined intent) was used in Study III and IV⁽⁹²⁻⁹⁴⁾. Combination of these codes intends to compensate for under-reporting of suicidal behaviour as well as geographical and temporal differences in ascertainment methods. Sensitivity analyses of excluding cases with undetermined intent were performed and similar results were observed. Suicide attempt was dichotomised as suicide attempt and no suicide attempt in all the studies.

Death due to suicide was an outcome measure in Study I, II, and IV in this thesis. In Study III suicide was used to define the study population. Suicide was measured according to ICD-10 X60-X84 in Study I and II. ICD-10 codes X60-X84 and Y10-Y34 were combined for suicide in Study III and IV. Sensitivity analyses of excluding cases with undetermined intent were performed and similar results were observed.

3.4 Statistical analyses

Descriptive statistics were performed in all the studies, including calculating frequencies and percentages, means with standard deviations, and medians. In Study I-III, proportions of the exposure measures, covariates and outcome measures were presented separately for women and men. Chi²-tests were used to test possible sex differences in Study II and III and cohort differences in Study IV.

Cox proportional hazards regression models were applied in Study I, II and IV to analyse the association between sickness absence and inpatient care due to mental and somatic disorders (Study IV), suicide attempt (Study I, II, and IV), and suicide (Study I, II, and IV) with crude and adjusted hazard ratios (HR) and 95% confidence intervals (CI). These models were applied after testing that the proportional hazard assumption was met. In Study I, the analyses were stratified by sex when the partial likelihood ratio test indicated an interaction with sex. In Study IV, the partial likelihood ratio test was performed in order to test an interaction between measures of sickness absence and the two cohorts in relation to the different outcome measures.

Individuals were followed until the event (inpatient care due to mental or somatic disorders, suicide attempt, death due to suicide), death (due to other reasons than suicide), emigration, or end of follow-up whichever came first in Study I, II, and IV. In Study I, follow-up time started from the first day of the first new sick-leave spell with benefits in 2005. Individuals with no sickness absence were followed from 1 January 2005. In Study II and IV, follow-up time was started after the exposure year for all individuals. Besides the crude model, a number of covariates were also adjusted for. In Study I, socio-demographic factors were

adjusted for in the first model, while additional information on previous mental health care from inpatient and specialised outpatient care, suicide attempt from inpatient care and current antidepressant prescription were considered in the final model. Similar as in Study I, in Study IV social-demographic factors were adjusted for in the first model and then previous and ongoing mental and somatic disorders from in- and specialised outpatient care, previous suicide attempt from inpatient care and current antidepressant prescription were additionally adjusted for. In Study II, multivariate models included socio-demographic, health care, medication, and sickness absence factors which were significantly related to the outcome in the crude model. Due to the collinearity of different measures of sickness absence, only sick-leave spells and sick-leave diagnoses were included in the multivariate models for suicide attempt and suicide, respectively (as these two sickness absence measures were strongest associated with the respective outcome). In addition, other sickness absence variables were separately taken into consideration in the models (excluding the previously mentioned ones) adjusting for socio-demographic factors, health care, medication, and suicide attempt.

In Study III, group-based trajectory modelling was used to estimate trajectories of sickness absence and disability pension from the time span of 5 years (T-5) to the time span of one year (T-1) before suicide. This procedure is based on a mixture model that provides the capacity to identify subgroups of individuals who follow distinct trajectories during the time of observation and estimates a regression model for each discrete group (171). The Bayesian information criterion (BIC) was applied to test the best-fitted model related to the number of groups, i.e. determine the optimal number of trajectory groups. The BIC scores are negative values in which those closer to 0 indicate a better fit of the model.

Multinomial logistic regression and χ^2 -tests were applied to estimate associations of socio-demographic and health care characteristics in each trajectory group of sickness absence and disability pension in Study III. Individuals with missing values in the variables on “education”, “type of region of residence”, and “family situation” were excluded when performing the χ^2 -test and the multinomial logistic regression. The likelihood ratio χ^2 -test in the multinomial logistic regression was used to assess whether socio-demographic and health care factors were associated with type of trajectory in the full model. Moreover, the Nagelkerke R^2 values were analysed to estimate the strength of the associations. By consecutively excluding each factor from the full model, differences in R^2 for each factor were calculated in order to examine the contribution of a given factor to the full model.

Statistical analyses were performed using statistical software SPSS for Windows V.20.0/22.0 and/or SAS for Windows version 9.4 (SAS-based procedure “Traj” (171)).

4 Results

The results of the four studies are presented below.

4.1 Study I

The cohort of Study I consisted of 4 923 404 individuals and there were 2 337 295 women (47.5%) and 2 586 109 men. Of the study population, 8.5% of the women and 5.2% of the men had at least one new sick-leave spell in 2005. In general, women had longer sick-leave spells than men. During the six years of follow-up, 0.4% of women and 0.3% of men attempted suicide, whilst 0.1% of men and 0.03% of women committed suicide.

Table 6. Crude and adjusted hazard ratios and 95% confidence intervals (CI) for suicide attempt, following a sick-leave spell in 2005 due to different sick-leave diagnoses among women and men.

Sick-leave, diagnostic categories	Suicide attempts	Model 0 ^a	Model 1 ^b	Model 2 ^c
	n (%)	Hazard ratios (95% CI)		
Women				
Mental diagnoses	972 (2.2)	6.16 (5.76-6.59)	8.42 (7.86-9.02)	2.98 (2.77-3.21)
Nervous diagnoses	21 (0.3)	0.95 (0.62-1.46)	1.54 (1.00-2.36)	1.31 (0.85-2.01)
Respiratory diagnoses	51 (0.4)	1.10 (0.84-1.45)	1.90 (1.44-2.50)	1.57 (1.19-2.07)
Digestive diagnoses	42 (0.7)	1.87 (1.38-2.54)	2.67 (1.97-3.61)	2.13 (1.57-2.89)
Musculoskeletal diagnoses	217 (0.5)	1.28 (1.12-1.46)	1.87 (1.64-2.15)	1.64 (1.43-1.88)
Symptoms and signs ^d	64 (0.7)	1.94 (1.52-2.49)	2.75 (2.15-3.52)	2.11 (1.65-2.70)
Injury and poisoning	94 (0.6)	1.57 (1.28-1.92)	2.38 (1.94-2.92)	2.08 (1.70-2.56)
No sickness absence	7890 (0.4)	1	1	1
Men				
Mental diagnoses	611 (2.8)	11.99 (11.03-13.03)	12.92 (11.88-14.07)	3.64 (3.32-4.00)
Nervous diagnoses	31 (1.0)	4.13 (2.90-5.87)	5.08 (3.57-7.23)	3.77 (2.65-5.37)
Circulatory diagnoses	32 (0.4)	1.61 (1.14-2.28)	2.59 (1.82-3.67)	2.16 (1.52-3.06)
Respiratory diagnoses	26 (0.3)	1.44 (0.98-2.12)	1.77 (1.20-2.60)	1.39 (0.94-2.04)
Digestive diagnoses	30 (0.4)	1.63 (1.14-2.34)	1.96 (1.37-2.80)	1.81 (1.26-2.59)
Musculoskeletal diagnoses	153 (0.4)	1.72 (1.46-2.01)	1.94 (1.65-2.28)	1.79 (1.53-2.11)
Injury and poisoning	151 (0.6)	2.51 (2.14-2.96)	2.39 (2.04-2.81)	2.13 (1.81-2.51)
No sickness absence	6111 (0.3)	1	1	1

^a Model 0: Crude.

^b Model 1: Adjusted for age, educational level, type of region of residence, country of birth, and family situation.

^c Model 2: Adjusted for age, educational level, type of region of residence, country of birth, family situation, previous in- and specialised outpatient care due to mental disorders, previous suicide attempt from inpatient care, and antidepressants in 2005.

^d Including abnormal clinical and laboratory findings.

All-cause sickness absence was associated with a higher HR of suicide attempt after adjusting for socio-demographic factors, previous mental health care and suicide attempt, and antidepressants among both women (HR 2.37; 95% CI 2.25-2.50) and men (HR 2.69; 95% CI 2.53-2.86).

Table 6 shows that the crude HR of suicide attempt among women was highest for those on mental sickness absence (HR 6.16; 95% CI 5.76-6.59), followed by sickness absence due to symptoms and signs, diagnoses of the digestive system, injury/poisoning, and diagnoses of the musculoskeletal system (range of HRs: 1.28-1.94). Among men, the crude HR of suicide attempt was also highest for mental sickness absence (HR 11.99; 95% CI 11.03-13.03). The other diagnoses of sickness absence which were associated with higher HRs of suicide

attempt among men were for instance diagnoses of the nervous system, injury/poisoning as well as diagnoses of the musculoskeletal and the digestive system (range of HRs: 1.44-4.13).

In the final models, the HRs were strongly reduced for mental sickness absence, somewhat stronger among men (Table 6). Still, significant results persisted among women (HR 2.98; 95% CI 2.77-3.21) and men (HR 3.64; 95% CI 3.32-4.00). The other sick-leave diagnoses which showed higher HRs of suicide attempt among women and men in the multivariate models included injury and poisoning, digestive diagnoses, and musculoskeletal diagnoses (range of HRs: 1.64-2.13). Additionally, women on sickness absence due to respiratory diagnoses and symptoms and signs had higher HRs of suicide attempt, while sickness absence due to diagnoses of the nervous system and the circulatory system was predictive of suicide attempt among men. The partial likelihood ratio test showed a significant interaction of sex and sickness absence due to mental diagnoses and diagnoses of the nervous system with regard to subsequent suicide attempt ($p < 0.001$). Sickness absence due to these diagnoses was associated with significantly higher HRs for subsequent suicide attempt in men than in women.

Table 7. Crude and adjusted hazard ratios and 95% confidence intervals (CI) for suicide, following a sick-leave spell in 2005 due to different sick-leave diagnoses among women and men.

Sick-leave, diagnostic categories	Suicide	Model 0 ^a	Model 1 ^b	Model 2 ^c
	n (%)	Hazard ratios (95% CI)		
Women				
Mental diagnoses	79 (0.2)	6.69 (5.29-8.46)	6.69 (5.26-8.49)	2.74 (2.12-3.53)
Musculoskeletal diagnoses	22 (0.05)	1.75 (1.14-2.68)	1.76 (1.15-2.70)	1.58 (1.03-2.43)
No sickness absence	585 (0.03)	1	1	1
Men				
Mental diagnoses	156 (0.7)	8.48 (7.20-9.97)	7.88 (6.69-9.28)	2.96 (2.48-3.54)
Musculoskeletal diagnoses	63 (0.2)	1.99 (1.55-2.56)	1.78 (1.38-2.29)	1.66 (1.29-2.14)
Injury and poisoning	46 (0.2)	2.15 (1.61-2.89)	1.91 (1.43-2.56)	1.76 (1.32-2.36)
No sickness absence	2193 (0.1)	1	1	1

^a Model 0: Crude.

^b Model 1: Adjusted for age, educational level, type of region of residence, country of birth, and family situation.

^c Model 2: Adjusted for age, educational level, type of region of residence, country of birth, family situation, previous in- and specialised outpatient care due to mental disorders, previous suicide attempt from inpatient care, and antidepressants in 2005.

Moreover, there was a higher HR of suicide attempt with increasing duration (sick-leave days) among women and men. The HR for suicide attempt was 3.35 among women with sickness absence longer than 365 days (95% CI 3.13-3.80) in the final model, while the HR of suicide attempt was 3.46 among men with sickness absence of 181-365 days (95% CI 2.93-4.08) after controlling for all covariates. In general, men with different sick-leave durations with the exception of more than 365 days had higher HRs of suicide attempts than women ($p < 0.05$).

Also for suicide high HRs were found among women and men on all-cause sickness absence in the crude models (Table 7). In the final models, higher risks of suicide were found among women (HR 1.91; 95% CI 1.60-2.29) and men (HR 1.92; 95% CI 1.71-2.14) on sickness absence compared to those without sickness absence. Table 7 shows that women and men

with sickness absence due to mental diagnoses had particularly high HRs of suicide. This pattern remained even after controlling for all covariates (women: HR 2.74; 95% CI 2.12-3.53; men: HR 2.96; 95% CI 2.48-3.54). Moreover, the risk estimates of suicide were 1.58 and 1.66 for women and men on sickness absence due to musculoskeletal diagnoses in the multivariate model. The HR of suicide was 1.76 for men on sickness absence due to injury and poisoning. Also, different sick-leave durations were predictive of suicide among women and men. The HR of suicide was 3.55 among women and 2.34 among men with sickness absence of 181-365 days.

4.2 Study II

The cohort in study II consisted of 12 647 women (59.9%) and 8449 men, who were treated in in- or specialised outpatient health care due to depressive disorders in 2005. During the five years of follow up, 1209 individuals attempted suicide while 152 individuals committed suicide. Regarding sickness absence in 2005, 31.5% had new (incident) sick-leave spells. Considerable proportions of individuals had only one new sick-leave spell (25.3%), had full-time sickness absence during all spells (16.8%), had more than 365 days of sickness absence of spells initiated in 2005 (11.6%), and new sick-leave spells due to mental diagnoses (25.0%).

In this study, a number of sickness absence measures, socio-demographic factors, health care factors as well as different types of medication were investigated in relation to subsequent suicide attempt and suicide. In the univariate models, most of the analysed factors were associated with higher HRs for suicide attempt and suicide. After adjusting for socio-demographics and health care factors, new sick-leave spells, full-time spells, spells exceeding 365 days, having 1 or more sick-leave spells, and spells due to mental diagnoses were found to be associated with higher HRs of suicide attempt (range of HRs 1.18-1.44) (Table 8).

In addition, in the multivariate models a higher risk of subsequent suicide attempt was found to be higher among women than among men. In contrast, male sex was associated with a two-fold higher risk of suicide than female sex. Young age (16-24 years old) was associated with a higher risk of attempting suicide (HR 1.47; 95% CI 1.21 to 1.78) compared with patients aged 35-44 years. Further, low and medium educational level, and living without a partner and without children were associated with higher HRs of suicide attempt. On the other hand, older age (45-64 years old), and living in small towns were observed to be associated with lower HRs of suicide attempt. Moreover, living with a partner and with children was associated with a lower HR of suicide.

Dispensed prescription of both antidepressants and anxiolytics showed a two-fold higher HR of suicide attempt and suicide compared with patients with no prescription of antidepressants or anxiolytics. Patients who were only prescribed antidepressants had a HR of 1.34 for suicide attempt. Hospital stay due to mental disorders during 2000-2005 and previous suicide attempt during 2000-2004 compared with no hospital stay and no previous suicide attempt was associated with two to three-fold higher HRs of suicide attempt and suicide. Also,

associations between long inpatient care stays due to somatic disorders and subsequent suicide attempt were observed, which showed HRs of 1.79 and 1.81 for suicide attempt.

Table 8. Crude and adjusted hazard ratios and 95% confidence intervals (CI) for suicide attempt in individuals who in 2005 had in- or specialised outpatient care due to depressive disorders, following a sick-leave spell in 2005 measured in different ways.

Sickness absence	n (%)	Model 0 ^a	Model 1 ^b
		Hazard ratios (95% CI)	
Sick-leave grade			
No sick-leave spell	513 (5.6)	1	1
Full-time ^c	257 (7.2)	1.32 (1.14-1.54)	1.32 (1.12-1.56)
Part-time	174 (5.6)	1.01 (0.85-1.20)	1.11 (0.91-1.34)
Length (days) ^d			
No sick-leave spell	513 (5.6)	1	1
1-90	119 (5.8)	1.06 (0.87-1.29)	1.22 (0.99-1.51)
91-365	127 (5.9)	1.08 (0.89-1.31)	1.08 (0.88-1.32)
>365	185 (7.5)	1.37 (1.16-1.62)	1.39 (1.15-1.68)
Number of spells			
No sick-leave spell	513 (5.6)	1	1
1 spell	330 (6.2)	1.12 (0.98-1.29)	1.18 (1.01-1.39)
≥2 spells	101 (7.7)	1.42 (1.15-1.76)	1.44 (1.15-1.81)
Sick-leave diagnoses			
No sick-leave spell	513 (5.6)	1	1
Spells with mental diagnoses ^e	363 (6.9)	1.25 (1.09-1.43)	1.25 (1.08-1.46)
Spells with somatic diagnoses	50 (4.8)	0.88 (0.66-1.17)	1.13 (0.84-1.53)
Spells with missing diagnoses	18 (5.5)	1.02 (0.64-1.64)	1.13 (0.71-1.82)
Sickness absence			
No sick-leave spell	513 (5.6)	1	1
Ongoing sick-leave spells ^f	265 (5.1)	0.91 (0.79-1.06)	1.03 (0.87-1.22)
New sick-leave spells	431 (6.5)	1.18 (1.04-1.34)	1.23 (1.06-1.43)

^a Model 0: Crude.

^b Model 1: Each sickness absence variable adjusted separately for socio-demographic, health care, and medication factors.

^c Full-time: in all sick-leave spells during 2005.

^d Length (days): sum of total days in all sick-leave spells during 2005.

^e Spells with mental diagnoses: at least one new sick-leave spell in 2005 with a mental diagnosis.

^f Ongoing sick-leave spells: without any new sick-leave spell and ongoing from the years preceding 2005.

4.3 Study III

The study population of this study consisted of 4209 individuals who committed suicide in the years 2007 to 2010. Five groups of different trajectories of sickness absence and disability pension (SA/DP) months during the five years prior to suicide were identified as the best fitting model by using the BIC-based procedure in the trajectory analyses (Figure 4). The five groups were labelled as follows: “Constant Low”, “Constant High”, “Increasing Low”, “Increasing High”, and “Decreasing”.

The “Constant Low” group consisted of a large proportion of individuals (46.4%) who committed suicide with constantly few months of SA/DP over the years prior to suicide. In total, 30.4% of individuals with high level of SA/DP belonged to the “Constant High” group. On average, they had more than 10 months of SA/DP annually. The “Increasing Low” and the “Increasing High” groups included 9.2% and 6.9% of the individuals with completed suicide, respectively. Both of the groups primarily had increasing SA/DP months during the time before suicide with different increasing patterns. The “Increasing Low” group started

with having a few SA/DP months five years before the suicide (T-5). In this group, SA/DP months increased only marginally up until the time span of 2 years before suicide (T-2), when the increase became sharp. On the other hand, the “Increasing High” group had a strong increase of SA/DP months from five years prior to suicide and onwards and continued with the strong increase until T-2. The “Decreasing” group consisted of 7.1% of the individuals and showed a decrease in SA/DP over the study period (Figure 4).

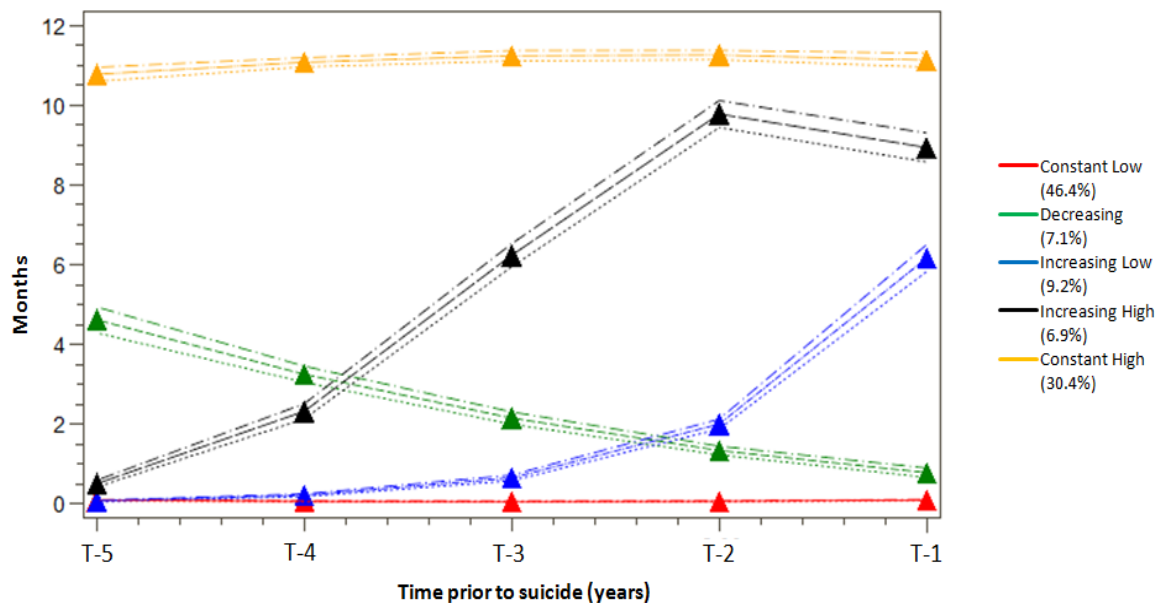


Figure 4. SA/DP trajectories during the five years (T-5 to T-1) prior to suicide, mean number of net SA/DP months per year.

Further, associations of socio-demographic and health care characteristics with the different trajectory groups were explored. All socio-demographic and health care factors were significantly associated with the trajectory groups ($P < 0.05$) with the exception of “country of birth” and “type of region of residence”. After controlling for all socio-demographic and health care factors in the full model, the significant results remained. Age had a more important role than other factors in the full model.

Younger men and individuals with higher education, who were adolescents living with their parents, as well as those who had neither mental nor somatic inpatient care nor suicide attempt were overrepresented in the “Constant Low” group. Still, as much as 43.8% of the individuals in this group had had specialised outpatient somatic health care with 1-2 visits at baseline. On the other hand, the “Constant High” group predominantly comprised older women and individuals with lower education and those with more health care and suicide attempts. There was a larger proportion of individuals of female sex, middle age (39-49 years), with high school education, and who were living alone with children included in the “Decreasing” group. With regard to health care characteristics, approximately 10-15% had attempted suicide or had mental or somatic in- or specialised outpatient care exceeding the median number of days or visits of the study population at baseline in the “Decreasing” group. The two groups with increasing SA/DP months showed somewhat different distributions of socio-demographic and health care characteristics. Compared to the

“Increasing High” group, individuals in the “Increasing Low” group tended to be younger, with higher education and with less somatic and mental health care.

4.4 Study IV

In this study the associations of sickness absence and subsequent morbidity and suicidal behaviour were investigated in two cohorts (one before and one after considerable changes in social insurance regulations in 2008). These cohorts (baseline in 2006 versus 2009) consisted of 4 477 678 and 4 500 400 individuals, respectively. During the two years of follow-up of the first cohort (2006), 30 986 individuals (0.7%) and 536 404 individuals (12.0%) were treated in inpatient health care due to mental and somatic disorders during 2007-2008, respectively. Moreover, 3350 individuals (0.1%) were admitted to inpatient care due to suicide attempt and 1821 individuals (0.04%) committed suicide during 2007-2008. In the latter cohort (2009), 34 843 individuals (0.8%) and 559 090 individuals (12.4%) had mental and somatic inpatient health care during follow-up, respectively. In total, 3579 individuals (0.1%) attempted suicide and 1232 individuals (0.03%) died due to suicide during 2010-2011. Individuals with sickness absence in the two cohorts were significantly different with regard to all measured characteristics and outcome measures with exception of sex and subsequent suicide.

Table 9. Crude and adjusted hazard ratios and 95% confidence intervals (CI) for mental inpatient health care, following the first new sick-leave spell due to mental diagnoses and long sick-leave duration, in 2006 and 2009, respectively.

Sickness absence	Inpatient mental care n (%)	Model 0 ^a	Model 1 ^b	Model 2 ^c
Hazard ratios (95% CI)				
Sickness absence in 2006				
Sick-leave diagnoses				
CMD ^d	2491 (3.8)	6.67 (6.40-6.95)	7.10 (6.81-7.40)	1.67 (1.59-1.74)
Other mental diagnoses	1074 (16.9)	32.05 (30.15-34.07)	27.11 (25.50-28.83)	2.39 (2.24-2.54)
Sick-leave duration				
>365 days	1450 (3.9)	6.82 (6.47-7.19)	7.29 (6.91-7.69)	1.86 (1.76-1.97)
No sickness absence	23 782 (0.6)	1	1	1
Sickness absence in 2009				
Sick-leave diagnoses				
CMD ^d	2326 (4.9)	7.34 (7.04-7.66)	7.83 (7.50-8.17)	1.64 (1.57-1.72)
Other mental diagnoses	984 (21.1)	35.56 (33.37-37.90)	29.39 (27.57-31.32)	2.33 (2.18-2.49)
Sick-leave duration				
>365 days	1025 (6.7)	10.39 (9.76-11.06)	10.57 (9.93-11.26)	2.02 (1.89-2.15)
No sickness absence	28 434 (0.7)	1	1	1

^aModel 0: Crude.

^bModel 1: Adjusted for sex, age, educational level, type of region of residence, country of birth, and family situation.

^cModel 2: Adjusted for sex, age, educational level, type of region of residence, country of birth, family situation, previous and ongoing inpatient and specialised outpatient care due to mental and somatic disorders, previous suicide attempt from inpatient care, and antidepressants in 2006/2009.

^dCMD: Common mental disorders.

All-cause and diagnosis-specific sickness absence as well as different sick-leave durations were associated with higher risks of mental inpatient health care compared to those without sickness absence in both cohorts in the univariate models (Table 9). The partial likelihood ratio test showed that individuals with sickness absence due to CMD and other mental diagnoses and sickness absence longer than 365 days in 2009 had higher HRs of subsequent

mental inpatient health care compared to those with such sickness absence in 2006 in the univariate models. After adjusting for socio-demographic factors, previous and ongoing health care factors, previous suicide attempt and antidepressant prescription, all sick-leave variables were still associated with higher HRs of subsequent mental inpatient care in both cohorts. The associations between sickness absence due to CMD and other mental diagnoses as well as sickness absence longer than 365 days with mental inpatient health care were attenuated more strongly among those on sickness absence in 2009 than those on sickness absence in 2006 after controlling for all covariates (Table 9).

Table 10. Crude and adjusted hazard ratios and 95% confidence intervals (CI) for somatic inpatient health care, following the first new sick-leave spell due to different diagnoses and long sick-leave duration, in 2006 and 2009, respectively.

Sickness absence	Somatic inpatient care	Hazard ratios (95% CI)		
	n (%)	Model 0 ^a	Model 1 ^b	Model 2 ^c
Sickness absence in 2006				
Sick-leave diagnoses				
CMD ^d	10 913 (16.8)	1.57 (1.54-1.60)	1.39 (1.36-1.42)	1.15 (1.13-1.17)
Musculoskeletal diagnoses	16 996 (18.8)	1.78 (1.75-1.81)	1.72 (1.69-1.75)	1.41 (1.38-1.43)
Sick-leave duration				
181-365 days	6538 (25.4)	2.57 (2.51-2.63)	2.41 (2.35-2.47)	1.79 (1.74-1.83)
>365 days	10 813 (29.0)	3.01 (2.95-3.07)	2.79 (2.73-2.84)	2.09 (2.05-2.13)
No sickness absence	450 397 (11.1)	1	1	1
Sickness absence in 2009				
Sick-leave diagnoses				
CMD ^d	8928 (18.7)	1.68 (1.65-1.72)	1.48 (1.45-1.51)	1.18 (1.16-1.21)
Musculoskeletal diagnoses	14 336 (21.1)	1.94 (1.90-1.97)	1.87 (1.84-1.91)	1.44 (1.41-1.46)
Sick-leave duration				
181-365 days	5680 (29.2)	2.91 (2.83-2.99)	2.74 (2.67-2.81)	1.86 (1.81-1.91)
>365 days	6015 (39.2)	4.29 (4.19-4.40)	3.97 (3.87-4.08)	2.59 (2.52-2.66)
No sickness absence	484 682 (11.6)	1	1	1

^aModel 0: Crude.

^bModel 1: Adjusted for sex, age, educational level, type of region of residence, country of birth, and family situation.

^cModel 2: Adjusted for sex, age, educational level, type of region of residence, country of birth, family situation, previous and ongoing inpatient and specialised outpatient care due to mental and somatic disorders, previous suicide attempt from inpatient care, and antidepressants in 2006/2009.

^dCMD: Common mental disorders.

In the crude model for somatic inpatient care, all-cause sickness absence, sickness absence due to CMD, and musculoskeletal diagnoses and other somatic diagnoses and sickness absence more than 14 days in 2009 were found to be associated with significantly higher risk estimates than such sickness absence in 2006. All-cause sickness absence, sickness absence due to CMD and musculoskeletal diagnoses as well as sick-leave duration longer than 180 days in 2009 remained to be associated with higher HRs of subsequent somatic inpatient health care compared to the HRs related to these sick-leave measures in 2006 after controlling for all covariates (Table 10).

Higher HRs of suicide attempt and suicide were found in relation to all-cause sickness absence, specific sick-leave diagnoses and sick-leave duration in both cohorts in the crude analyses. Especially, sickness absence due to CMD and other mental diagnoses as well as sick-leave durations >90 days showed prominently high HRs of subsequent suicide attempt and suicide. The high risk estimates of suicide attempt remained in most of the sick-leave variables after adjustment for all covariates, with few exceptions. The HRs of subsequent

suicide attempt were notably higher for those with sickness absence of more than 365 days in 2006 and 2009 (HR 2.14; 95% CI 1.84-2.50 vs. HR 1.82; 95% CI 1.46-2.27). For suicide, higher HRs were found related to sickness absence due to CMD in 2006 and 2009 and sickness absence due to other mental diagnoses in 2006 compared to those without sickness absence in the respective cohort. Sick-leave duration in 2006 was associated with higher risks of suicide except for sick-leave days longer than 365 days. Moreover, 15-365 days of sickness absence in 2009 was associated with higher HRs of suicide than those without sickness absence after controlling for all covariates.

5 Discussion

5.1 Main findings

The main findings in this thesis include that mental and specific somatic sickness absence as well as sick-leave duration were associated with higher risks of subsequent suicide attempt and suicide among both women and men compared to individuals without a new sick-leave spell. Analyses were adjusted for socio-demographic factors, health care, and medication. An association was also found between sickness absence, which was measured in different ways, and subsequent suicide attempt among patients with depressive disorders from in- or specialised outpatient care. Here, patients with depressive disorders on full-time sick-leave spells, spells exceeding one year, mental sickness absence, and those having one or more sick-leave spells had a higher risk of suicide attempt compared to those without sickness absence, after adjustment for all covariates. Associations between sickness absence and subsequent morbidity and suicidal behaviour were observed similarly before and after considerable changes of the social insurance regulations in Sweden in 2008. Still, sickness absence due to CMD and musculoskeletal diagnoses and sickness absence longer than 180 days in 2009 were associated with higher HRs of subsequent somatic inpatient care than such sickness absence in 2006. Five different trajectory groups of SA/DP during the five years prior to suicide were identified. Almost half of those who committed suicide had constantly low levels of SA/DP during those five years, while 30% had constantly high levels of SA/DP before their suicide. The different trajectories were associated with different socio-demographic profiles and health care factors five years before suicide. The distributions of these characteristics were particularly different in the group with constantly low as opposed to constantly high SA/DP levels.

5.2 Discussion of results

The main findings of this thesis are discussed below.

5.2.1 Sick-leave diagnoses and subsequent morbidity/suicidal behaviour

Mental disorders are common among individuals with suicidal behaviour. Studies in this thesis showed that sickness absence due to mental diagnoses, including CMD and other mental diagnoses was also a prominent risk marker for later suicide attempt and suicide not only in the general population but also in patients with depressive disorders from in- or specialised outpatient care. This association was also found with regard to sickness absence measured before and after the regulatory changes in Sweden in 2008. The findings are consistent with previous studies, reporting higher risk of suicidal behaviour among sickness absentees with mental diagnoses (15, 153, 155). The finding on sickness absence being a marker of subsequent suicidal behaviour also in depressed patients has not been reported before. It is of particular note that sickness absence which was measured in different ways was an equally strong risk factor for subsequent suicidal behaviour as a number of well-established risk markers in depressed patients, e.g., female sex for subsequent suicide attempt (85).

In men, sickness absent due to mental diagnoses was found to be associated with a somewhat higher HR of subsequent suicide attempt compared to the risk estimate among women. Also,

the risk estimates of future suicide attempt were more strongly reduced among men with mental sickness absence after controlling for all covariates, than among women. This might suggest that men might have a higher severity of the underlying mental disorder when sickness certified with mental diagnoses. Sex differences in the prevalence and clinical manifestations of mental disorders, a higher threshold among men for reporting and seeking help due to mental complaints, and a gender bias in health care regarding identifying mental disorders, may partly explain the observed sex differences (172-174).

Moreover, higher risks of suicide attempt and suicide among individuals with sickness absence due to a number of different somatic diagnoses were found compared to those without sickness absence (Study I). For example, findings showed higher HRs of suicide attempt and suicide among individuals with sickness absence due to musculoskeletal diagnoses. This finding corresponds with a previous study, which reported a higher risk of suicide related to sickness absence due to musculoskeletal diagnoses compared to those without sickness absence (152). In addition, many somatic disorders often occur with pain and/or psychosocial stress in case of fatal somatic disorders and limitations in social life, which may result in a higher risk of suicidal behaviour (119). Other potential explanations for the association of somatic sickness absence include a co-occurring or unrecognised mental disorder (175). Unmeasured residual confounding of an underlying mental disorder might be possible in this study. Information on mental disorders which were treated outside of specialised healthcare or not treated with antidepressants, as well as undetected and untreated mental disorders was not available. Thus, it is possible that unrecognised or unmeasured comorbid mental disorders underlie the association of somatic sickness absence and subsequent suicidal behaviour.

Association between somatic sickness absence and later suicidal behaviour was also found to be sex specific in Study I. A two-fold risk of suicidal behaviour in men on sickness absence due to injury/poisoning was observed compared to men without sickness absence. This might be explained by underlying alcohol abuse or dependence being more frequent in men than in women and being related to both injuries and suicidal behaviour (176). Also, a higher risk of suicide attempt in women sickness absent due to symptoms and signs than women without sickness absence was found. This diagnostic group may include, for instance, chronic fatigue syndrome, which is more prevalent in women than in men, and probably associated with a considerable degree of depression as well as functional impairment and disability with regard to social, physical and occupational aspects (177). Moreover, men on sickness absence due to diagnoses of the nervous system had higher HRs of subsequent suicide attempt than women. Previous studies regarding this association have reported inconsistent findings (119). Future studies are needed to investigate potential sex differences in the association of sickness absence due to somatic diagnoses with subsequent suicidal behaviour.

An association between diagnosis-specific sickness absence and inpatient care due to mental and somatic disorders was found (Study IV). This is in line with previous studies reporting higher risks of depression and sub-optimal health related to diagnosis-specific sickness absence compared to individuals not on sickness absence (14, 16). Additional findings from

Study IV suggest that sickness absence due to CMD in 2009 was associated with a higher HR of subsequent somatic inpatient care than sickness absence due to CMD in 2006. In this thesis, sickness absence has been measured before and after the considerable changes in the social insurance regulations in 2008. These findings might reflect that individuals on sickness absence due to CMD after the regulatory change were more likely to have a higher medical severity or any comorbid somatic disorders than those with such sickness absence before the new regulation was introduced.

Moreover, the high HRs of inpatient care due to mental disorders among sickness absentees due to mental diagnoses in 2009 were more strongly reduced after additionally adjusting for health care factors and antidepressant prescription than among those on mental sickness absence in 2006 (Study IV). These findings suggest that individuals on sickness absence in 2009 might also have had a higher severity of the underlying mental disorders compared to those with sickness absence in 2006. The descriptive statistics in Study IV showed that a larger proportion of individuals on sickness absence in 2009 had antidepressants prescription, longer inpatient care, more frequent outpatient care as well as previous suicide attempt than those on sickness absence in 2006. Still, reasons for a potentially higher medical severity in sickness absentees in 2009 compared to those in 2006 remain to be explained. A possible explanation includes the fact that the new regulations introduced in 2008 implied stricter rules for granting disability pension, which might have resulted in individuals with higher medical severity being sickness absent in 2009 than in 2006.

5.2.2 Sick-leave measures and subsequent morbidity/suicidal behaviour

Both the duration of the first new sick-leave spell in Study I and IV and sick-leave length of all sick-leave spells initiated during a year in Study II were found to be associated with higher HRs of suicide attempt and suicide. To our knowledge, this is the first study addressing sick-leave duration and length as risk markers for subsequent suicide attempt, while such an association has been previously reported for suicide (11, 149, 153). In Study IV, the results showed that increasing duration of the first new sick-leave spell was associated with a higher risk of subsequent inpatient care compared to not having a new sick-leave spell. This finding is consistent with previous studies, reporting an association between long sick-leave duration and subsequent morbidity (16, 18).

Higher HRs of hospitalisation due to somatic disorders among individuals with a long sick-leave duration (>180 days) in 2009 than those sickness absent in 2006 were found. To the best of our knowledge, this is the first study to compare two cohorts before and after the new social insurance regulations introduced in Sweden with regard to subsequent health outcomes. Generally, the new rules implied that eligibility for sick-leave benefits was limited to one year (2). Still, individuals with serious disease and reduced work capacity can be granted sickness benefits for a longer time (2). Hence, individuals with sick-leave duration exceeding one year in 2009 may have a higher medical severity and/or work incapacity related to the sickness absence than those in 2006. This might have resulted in the higher risk estimates of subsequent morbidity related to sickness absence in 2009 than in 2006.

In Study II, sickness absence was also measured in different ways. A higher risk of attempting suicide was found among those with full-time sickness absence and among those with one or more sick-leave spells compared to those without sickness absence. One previous study showed associations between more than one sick-leave spell and subsequent suicide attempt in individuals with sickness absence due to stress-related mental disorders (178). More sick-leave spells, full-time sickness absence, as well as longer sick-leave duration/length might not only be indicators of the severity of the disease, but might also entail social isolation and changes in health behaviour (e.g., high alcohol and tobacco use, little physical exercise) (3, 4). This might have an effect on the aggravation of symptoms and increase suicidal behaviour (3, 4). Future research is required to scrutinise these different measures of sickness absence as risk indicators for suicide attempt and suicide by taking the severity of symptoms as well as eventual comorbidity into account.

5.2.3 Trajectories of sickness absence and disability pension before suicide

In Study III, five different trajectories of SA/DP in the five years prior to suicide were identified. This may reflect the general knowledge that suicide victims consist of a heterogeneous group with regard to etiology, health care seeking behaviour, the suicidal process, and underlying diseases (83). In this study, a large proportion (46.5%) of the individuals either showed stable high levels (30.4%) or increasing number (16.1%) of annual SA/DP months preceding suicide. Individuals with high/stable levels had a mean of 10 SA/DP months annually. This is the first study, also internationally, investigating trajectories of SA/DP months prior to suicide. Recent studies focusing on such trajectories before first diagnosis of multiple sclerosis and of diabetes, respectively, found lower levels of work incapacity, i.e., SA/DP months compared to the findings related to individuals completing suicide (179, 180). A Swedish cohort of individuals with multiple sclerosis reported a proportion of around 23% with increasing and constant high levels of SA/DP months prior to first diagnosis (179). The mean of annual months related to the group with high levels of SA/DP was around 10 months. Another study which investigated two cohorts, i.e., a Finnish (<29%) and a French (<13%) occupational cohort reported much lower proportions of high/increasing work incapacity in individuals prior to first diagnosis of diabetes (180). Also lower levels of SA/DP prior to diabetes diagnoses were reported. High levels of SA/DP can here be regarded to be associated with the type and severity of the underlying diagnoses of SA/DP (50, 181). As discussed above, a large proportions of individuals with completed suicide suffer from mental disorders (83), and individuals with high and stable work incapacity before suicide might here reflect a group of patients with severe mental disorders.

On the other hand, approximately half of the individuals with completed suicide (46.4%) had few SA/DP months before suicide. This compares to higher proportions of individuals with low levels of work incapacity prior to multiple sclerosis in a recent study based on a Sweden cohort (>50%), and prior to first diagnosis of diabetes in a study based on a Finnish (>70%) and a French (>80%) occupational cohort (179, 180). Obviously, trajectories of SA/DP prior to suicide and/or prior to the first diagnosis of specific chronic diseases can be assumed to

differ. More research on work incapacity trajectories prior and post non-fatal self-harm behaviour and specific mental disorders is warranted.

5.2.4 Factors associated with sickness absence/disability pension and suicidal behaviour

Results in Study III showed that several socio-demographic factors were associated with different trajectories of SA/DP. Age showed the strongest associations. This is in line with previous studies reporting that SA and DP rates increase with age (37). It is thus reasonable to find higher proportions of older individuals in the “Constant High” group with many months of SA/DP prior to suicide whereas higher rates of younger people were found in the “Constant Low” group with few SA/DP months at T-5.

Also, socio-demographic factors were found to be risk markers for suicide attempt and suicide, including sex, age, education, and family situation in patients with depressive disorders (Study II). Female sex, young age, low and medium educational level, and being single without children living at home were risk markers of suicide attempt while living in small towns/villages was associated with a lower risk of suicide attempt among patients with depressive disorders. Male sex showed an excess risk of suicide while being married/cohabiting and having children living at home was a protective factor of suicide among patients with depressive disorders. These findings are in line with previous studies (182, 183). Still, the study on depressed patients in this thesis was based on a larger study population and had, therefore, more precise estimates than previous studies.

Measures of morbidity, i.e., in- and specialised outpatient health care and previous suicide attempt, were found to be both associated with SA/DP trajectories prior to suicide (Study III) and being predictors of suicidal behaviour in depressed patients in Study II. In Study III, high proportions of long mental and somatic inpatient care stays and more frequent outpatient visits measured five years prior to suicide (T-5) were found both in the “Constant High” and “Increasing High” groups. These measures reflect the severity of the underlying somatic and mental disorders. Moreover, the “Decreasing” group had a high level of health care use at T-5. The decreasing SA/DP months from T-5 to the year of suicide might reflect improvements in health conditions during the follow-up time. In Study II, inpatient care due to mental or somatic disorders was observed to be associated with a higher risk of subsequent suicide attempt and suicide among patients with depressive disorders compared to those without such care. Long hospital stays due to mental disorders may indicate a higher severity of the depressive disorder or another coexisting mental disorder, which has previously been shown to be associated with a higher risk of suicidal behaviour (83, 182).

In contrast, in Study III the “Constant Low” and the “Increasing Low” groups included a larger proportion of individuals with less in- and specialised outpatient care at T-5. The few SA/DP months at T-5 in the “Increasing Low” group could be interpreted by better health conditions in terms of less in- or specialised outpatient health care five years prior to suicide. The increasing number of average months with SA/DP in the “Increasing Low” group might signal deteriorations in somatic or mental health, which is reflected in increasing work

incapacity. Regarding the “Constant Low” group, one possible explanation of the lower health care use is that the group also comprised a larger proportion of young men. Young men have been reported to have a higher threshold for reporting health complaints and are less prone to seek help than their female counterparts (172, 173). Young men have also been reported to have less frequent previous suicide attempts than females when they commit suicide (184). Still, in this “Constant Low” group 43.8% of the individuals had specialised outpatient visits due to somatic disorders at T-5. Also in Study II, higher HRs of suicide attempt among individuals with somatic inpatient care were found. These results may be explained by the psychosocial stress associated with the medical severity of the underlying somatic disorder or unmeasured underlying comorbid mental disorders, which may be associated with subsequent suicidal behaviour (119).

Previous suicide attempt was found to be significantly associated with SA/DP trajectories prior to suicide in Study III and subsequent suicide attempt and suicide among patients with depressive disorders in Study II. These findings are consistent with previous studies showing higher risks of suicidal behaviour among depressed individuals with a history of attempted suicide than those without such a history (95, 104, 182, 183).

Further, a higher risk of suicide attempt and suicide was observed among patients with depressive disorders who were prescribed antidepressants in combination with anxiolytics (Study II). Physicians use antidepressants to treat patients with depressive disorders and anxiety disorders (185). Supplementary medication with anxiolytics may be used to treat insomnia and anxiety (185). Depressive disorders are often comorbid with anxiety and this comorbidity also occurs in individuals with suicidal behaviour (185, 186). Therefore, the higher risk of suicidal behaviour in patients with depressive disorders in case of combined prescription of antidepressants and anxiolytics may not only reflect the severity of depressive symptoms but also acute anxiety.

5.3 Methodological considerations

There are different methodological aspects that can be discussed regarding this type of epidemiological studies.

One such aspect is validity. The internal validity of a study can be violated by selection bias, information bias, or confounding (187). Selection bias refers to the fact when a proper randomised selection of individuals is not achieved and the sample is not representative for the population it is derived from (187). Selection bias is assumed to be low in the studies of this thesis since register data with national coverage was used including all people of working ages registered as living in Sweden, not a sample. However, information might be missing regarding some of the studied aspects in some of the used registers. For instance, around 20% of the diagnoses are missing for the visits in the specialised outpatient care derived from the National Patient Register in Sweden during the years 2001-2007 (167). According to a report on this, the rate of missing information on mental diagnoses varied between counties and was higher from private health care providers (167). Still, there is no reason to anticipate that individuals with a depressive disorder - that is, those building the study base of Study II -

represent a specific selection of individuals treated with these disorders in specialised outpatient health care in Sweden, as missing information is geographically randomly distributed.

Another methodological aspect includes information bias, which refers to a misclassification of exposure or outcome measures (187). This misclassification can be differential and non-differential. For exposure misclassification, differential misclassification can be assumed if the misclassification of the exposure is different between individuals with and without the outcome. In the contrary, non-differential misclassification is assumed if it is not related to the outcome. Same standards are used in the case of outcome misclassification.

One typical form of differential misclassification is recall bias, which is not an issue when using register data, as in this thesis (187). Additionally, the quality of the Swedish registers is considered to be good (90, 188) minimising the risk of information bias. Still, misclassifications of sick-leave diagnoses have been discussed, however seldom studied. Physicians state the main diagnosis that has led to the impaired work capacity in terms of ICD-codes at the sick-leave certificate. In some cases the information about diagnoses might not have been coded into ICD-codes by the physician, or has been difficult to read or scan at SIA, e.g. due to unreadable handwriting (189). Nevertheless, the validity of sick-leave diagnoses was evaluated in one study and showed acceptable validity (190). Moreover, missing information on sick-leave diagnoses in the MiDAS database was observed, that is, the diagnoses on the sickness certificate was not included in MiDAS (around 15% of all sick-leave spells after 2004). This mainly occurred for the very short sick-leave spells. However, missing information on sick-leave diagnoses in MiDAS appears to be randomly distributed across the different outcome measures and this misclassification is assumed to be non-differential. Furthermore, under-reporting of sickness absence due to mental diagnoses may be possible. On the other hand, the validity of mental sick-leave diagnoses can be assumed to be good if considering the stigma still attached to mental disorders (191).

In the data for this thesis, sick-leave spells <15 days were not included for most of the employed individuals since information on sickness absence for these individuals is only available for day 15 and onwards from the SIA (2). In Study I and IV, sick-leave duration 1-14 days mainly included unemployed individuals and individuals with some chronic diseases who might have higher risks of subsequent morbidity and suicidal behaviour. That means that risk estimates of sick-leave spells <15 days in relation to subsequent morbidity and suicidal behaviour in the studies might be overestimated.

Data on suicide attempt and suicide were obtained from the National Patient Register and the Cause of Death Register, both held by the National Board of Health and Welfare. Information on main diagnoses and causes of death is missing in around 1% of the cases in these registers (84, 90). In Study I and II, information on suicide attempt and suicide with determined intent was used. In Study III and IV, a strategy of combining suicide attempt and suicide with determined and undetermined intent was applied when defining suicidal behaviour (92-94, 167). Sensitivity analyses by excluding suicidal behaviour with undetermined intent showed similar results. Under-reported or misclassified suicide attempts and suicides may still occur. The

distribution of under-reported or misclassified suicidal behaviour may in some cases differ in relation to the exposure measures and in that case estimates might have been under- or overestimated.

A confounding variable is defined as being associated with both the exposure and the outcome and is not in the causal pathway between exposure and outcome (187). For this reason, confounders need to be taken into consideration in the analyses in order to estimate a relatively more accurate association. In the four studies, a number of potential confounders, including socio-demographic factors, inpatient and specialised outpatient care due to mental and somatic disorders, suicide attempt, and medication could be controlled for. Still, residual confounding is possible. For example, adjustment for psychiatric morbidity including information on antidepressant and/or anxiolytics prescription as well as specialised psychiatric health care does not capture all psychiatric morbidity. This means that information on psychiatric morbidity treated in primary health care, other prescription than antidepressants and anxiolytics and on morbidity which has not come to the attention of the health care system could not be controlled for in the analyses. Moreover, with regard to somatic morbidity only information on specialised health care was available. In addition, only previous suicide attempt from inpatient care was controlled for in the multivariate analyses. This can be seen both as a strength and as a limitation—a strength as the studies in this thesis captured the more serious cases. However, not all suicide attempters have been treated in inpatient care (85).

External validity refers to the generalisability of a finding to the general population (187). The study populations for all the studies in this thesis were defined by using registers with nationwide coverage and included the whole working-aged population, not a sample. The studies in this thesis are therefore not selected with regard to e.g., specific regions or specific occupational groups. Therefore, the findings in this thesis can be generalised to working-aged individuals living in countries with comparable economic and labour market situation and health care and social insurance systems. Measures of morbidity have been conceptualised as inpatient and specialised outpatient care (in some cases as prescribed psychotropic drugs) in the studies in this thesis. In Study II, e.g., depressive disorders were measured by in- or specialised outpatient care due to these disorders. Findings in Study II can, therefore, be generalised to patients with these disorders treated in specialised health care in countries with comparable health care systems.

5.4 Conclusions

- All-cause sickness absence was associated with higher hazard ratios (HR) of subsequent suicide attempt and suicide among individuals of the general population as well as among patients with depressive disorders than among people without sickness absence. Although more women are usually granted sickness benefit, the risk of subsequent health outcomes and suicide mortality seems comparable for both women and men with sickness absence. Furthermore, higher HRs related to all-cause sickness absence were found regarding subsequent mental and somatic inpatient health care in the general population when comparing those with and without sickness absence.

- Sickness absence due to mental diagnoses was a risk marker for subsequent inpatient health care, suicide attempt, and suicide among women and men in the general population and both before and after the changes of social insurance regulations in 2008 in Sweden, as well as in patients with depressive disorders. Moreover, individuals with incident sickness absence due to mental diagnoses in 2009 had higher HRs of subsequent inpatient care due to somatic disorders than individuals with such sickness absence in 2006. This might be related to differences in the severity of the underlying mental disorders in individuals on sickness absence before and after the regulatory changes in 2008 in Sweden. The new stricter rules may be related to the higher medical severity in individuals who were granted sickness benefit due to mental diagnoses after 2008.
- Sickness absence due to somatic diagnoses was associated with higher HRs of subsequent inpatient health care, suicide attempt, and suicide among women and men in the general population (both before and after the regulatory changes in 2008) as well as in patients with depressive disorders compared with those without sickness absence. Specific somatic sick-leave diagnoses including musculoskeletal, injury, nervous, and circulatory disorders were associated with subsequent suicidal behaviour. Unmeasured and/or unrecognised mental disorders may underly these associations, highlighting the importance of the comorbidity of mental and somatic disorders.
- Higher HRs of subsequent suicide attempt and suicide were found in relation to long sickness absence duration among women and men of the general population and patients with depressive disorders. Moreover, full-time sickness absence and more sick-leave spells were associated with higher HRs of subsequent suicide attempt among patients with depressive disorders. Individuals on long-term sickness absence after the regulatory changes in 2008 had higher risks of subsequent inpatient care due to somatic disorders than individuals with such sickness absence before the regulatory changes. This may reflect the new regulation in 2008 which introduced stricter rules for granting sickness absence and disability pension and a time limitation for sickness absence.
- Among those who had committed suicide, five different trajectories of their sickness absence and disability pension (SA/DP) were identified during the five years before the suicide. Almost half of the study population had had constantly low levels of SA/DP, while 30% had constantly high levels of SA/DP before the suicide. These differences might be partly explained by the differences in socio-demographic and health care factors five years before suicide.
- Several socio-demographic, health care, and medication factors were associated with the five different previous SA/DP trajectories among individuals who had committed suicide. In the study of patients with depressive disorders, these factors were also associated with future suicide attempt and suicide.

5.5 Further research

Since associations between diagnosis-specific sickness absence and subsequent inpatient care and suicidal behaviour were found, it would be fruitful to conduct in-depth analyses regarding health care, medication, and different social situations in further studies. This

should be done stratified for different groups and including also information on changes of such aspects over time. Information on severity as well as on comorbidity also needs to be included in such studies. Future studies would also benefit from having information on primary health care use, and from self-reported health conditions, use of medication etc., and life style factors. In this way, a better knowledge on the extent to which the diagnosis of sickness absence contributes to higher risk of future adverse health outcomes would be gained. Studies that differentiate the effect of having a specific disease from being sickness absent due to that disease are challenging to design; however, possibilities to do this need to be further explored. Future studies are also recommended to use, for instance, surveys to collect information which could not be included in the studies of this thesis, e.g. information on morbidity of individuals who did not seek or require treatment in specialised health care.

Further, small sex differences and cohort differences were found regarding diagnosis-specific sickness absence and sick-leave duration with regard to subsequent suicidal behaviour and adverse health outcomes. There is a need of future studies to replicate these findings and investigate potential mechanisms between women and men and cohort differences in such associations. These studies should ideally have long follow-up periods in order to guarantee sufficient statistical power related to the analyses of rare outcomes like suicidal behaviour. Moreover, other statistical methods could be applied in order to elucidate potential period effects related to the new social insurance regulations.

As different SA/DP trajectories were found before suicide, further investigations of such trajectories are needed. Potential differences with regard to SA/DP trajectories prior to suicide attempt or first diagnosis of specific mental disorders as compared to SA/DP trajectories prior to completed suicide could be addressed in further research.

6 Acknowledgements

Working on the thesis has been a wonderful and often challenging experience. It has been an unbelievable journey in my life and I am indebted to many people for making the time working on my thesis an unforgettable experience.

First and foremost, I am deeply grateful to my principal supervisor associated professor *Ellenor Mittendorfer-Rutz* for accepting me as your doctoral student at the Division of Insurance Medicine. To work with you has been a real pleasure to me, with heaps of fun and excitement. Thank you so much for sharing your vast knowledge in epidemiology, psychiatric morbidity, and suicidal behaviour and for encouraging my research and for allowing me to grow as a research scientist. Your advice on both research as well as on my career have been invaluable, which I appreciate from my heart.

Furthermore, I am very grateful to my co-supervisors professor *Kristina Alexanderson* and professor *Bo Runeson*. To Kristina, thank you for providing and keeping a pleasant and productive working atmosphere, for sharing your profound knowledge in sickness absence research and the Swedish social insurance system, for your guidance and help with academic writing, and for the motivating discussions in the research area of insurance medicine, which has been inspiring for me. To Bo, thank you for sharing your expertise and knowledge regarding suicidal behaviour and for inviting me to present my research and to attend the Journal Clubs in your research group. I also very much appreciated that you very actively engaged in all my manuscript seminars and kappa seminar and gave great insights to all my works.

In addition, I want to thank all my co-authors who contributed and gave valuable inputs to the papers: *Jenny Head*, *Maria Melchior*, *Aleksander Perski*, *Charlotte Björkenstam*, and *Petter Tinghög*. To Charlotte and Petter, I want to thank you for patiently teaching me how to conduct the group-based trajectory analyses in SAS programming and the multinomial logistic regression.

During the four years of doctoral education, I felt very comfortable and enjoyed to work with all my colleagues at the Division of Insurance Medicine. Thanks for your support and input related to manuscripts and conference presentations. Especially, I am grateful to all the opponents of my manuscript seminars and the kappa seminar: *Birgitta Floderus*, *Pia Svedberg*, *Syed Rahman*, *Petter Tinghög*, *Lisa Mather*, *Magnus Stenbeck*, *Michael Wiberg*, *Marie Nilsson*, and *Marjan Vaez*. I would also like to acknowledge *Annika Evolahti* and *Katarina Lönnqvist* for the important administrative work you have done at the Division. To Annika, also thank you for proofreading my thesis. In addition, I want to thank all the statisticians who contributed to the data management of the data I have used: *Elin Hinas*, *Linnea Kjeldgård*, *Michael Wiberg*, and *Kerstin Nilsson*.

I am also thankful for the financial support from the *Swedish Research Council* and *Karolinska Institutet funds for doctoral education*.

I would also like to give heartfelt thanks to my mentor professor *Andrzej Werbart*. You have been an invaluable support during these four years. Thank you for listening, for your encouragement, and advice for research and for my career.

My gratitude is also extended to all my friends who were an amazing source of support and were by my side in every important moment of my life. I want to especially thank *Ke Zhang*, who shared an apartment with me during the first two years of my doctoral education and whom I consider to be my best friend. Thank you for always being my best supporter and sharing your life with me.

Finally, I would especially like to thank my family: my dear parents, aunt and uncle for their infinite support throughout everything. 感谢多年来妈妈爸爸和大姨大姨夫给予的支持与关爱! To my husband *Qiang Li*, we met after the first year of my doctoral education and I will never forget that you unexpectedly appeared at my half-time seminar without telling me in advance. Thank you for your patience and tolerance, and for all the surprises, support, and help you have brought to my life.

7 References

1. Alexanderson K, Norlund A. Swedish Council on Technology Assessment in Health Care (SBU). Chapter 1. Aim, background, key concepts regulations, and current statistics. *Scand J Public Health*. 2004;32(Supplement 63):12-30.
2. Social Insurance in Figures 2015. The Swedish Social Insurance Agency. 2015.
3. Vingård E, Alexanderson K, Norlund A. Swedish Council on Technology Assessment in Health Care (SBU). Chapter 9. Consequences of being on sick leave. 2004;32(Supplement 63):207-15.
4. Floderus F, Göransson S, Alexanderson K, Aronsson G. Self-estimated life situation in patients on long-term sick leave. *J Rehabil Med*. 2005;37:291-9.
5. Bryngelson A. Long-term sickness absence and social exclusion. *Scand J Public Health*. 2009 Nov;37(8):839-45.
6. Ferrie JE, Vahtera J, Kivimaki M, Westerlund H, Melchior M, Alexanderson K, et al. Diagnosis-specific sickness absence and all-cause mortality in the GAZEL study. *J Epidemiol Community Health*. 2009 Jan;63(1):50-5.
7. Head J, Ferrie JE, Alexanderson K, Westerlund H, Vahtera J, Kivimaki M. Diagnosis-specific sickness absence as a predictor of mortality: the Whitehall II prospective cohort study. *BMJ*. 2008;337:a1469.
8. Kivimaki M, Forma P, Wikstrom J, Halmeenmaki T, Pentti J, Elovainio M, et al. Sickness absence as a risk marker of future disability pension: the 10-town study. *J Epidemiol Community Health*. 2004 Aug;58(8):710-1.
9. Lund T, Kivimaki M, Labriola M, Villadsen E, Christensen KB. Using administrative sickness absence data as a marker of future disability pension: the prospective DREAM study of Danish private sector employees. *Occup Environ Med*. 2008 Jan;65(1):28-31.
10. Mittendorfer-Rutz E, Kjeldgård L, Runeson B, Perski A, Melchior M, Head J, et al. Sickness Absence Due to Specific Mental Diagnoses and All-Cause and Cause-Specific Mortality: A Cohort Study of 4.9 Million Inhabitants of Sweden. *PloS One*. 2012;7(9):1-9.
11. Vahtera J, Pentti J, Kivimaki M. Sickness absence as a predictor of mortality among male and female employees. *J Epidemiol Community Health*. 2004;58(4):321-6.
12. Laaksonen M, He L, Pitkaniemi J. The durations of past sickness absences predict future absence episodes. *J Occup Environ Med*. 2013 Jan;55(1):87-92.
13. Lund T, Kivimaki M, Christensen KB, al. e. Socio-economic differences in the association between sickness absence and mortality: the prospective DREAM study of Danish private sector employees. *Occup Environ Med*. 2009 Mar;66(3):150-3.
14. Melchior M, Ferrie JE, Alexanderson K, Goldberg M, Kivimaki M, Singh-Manoux A, et al. Using sickness absence records to predict future depression in a working population: prospective findings from the GAZEL cohort. *Am J Public Health*. 2009 Aug;99(8):1417-22.
15. Melchior M, Ferrie JE, Alexanderson K, Goldberg M, Kivimaki M, Singh-Manoux A, et al. Does sickness absence due to psychiatric disorder predict cause-specific mortality? A 16-year follow-up of the GAZEL occupational cohort study. *Am J Epidemiol*. 2010 Sep 15;172(6):700-7.
16. Vahtera J, Westerlund H, Ferrie JE, Head J, Melchior M, Singh-Manoux A, et al. All-cause and diagnosis-specific sickness absence as a predictor of sustained suboptimal health: a 14-year follow-up in the GAZEL cohort. *J Epidemiol Community Health*. 2010 Apr;64(4):311-7.
17. Alexanderson K, Kivimaki M, Ferrie JE, Westerlund H, Vahtera J, Singh-Manoux A, et al. Diagnosis-specific sick leave as a long-term predictor of disability pension: a 13-year follow-up of the GAZEL cohort study. *J Epidemiol Community Health*. 2012 Feb;66(2):155-9.
18. Ferrie JE, Kivimaki M, Westerlund H, Head J, Melchior M, Singh-Manoux A, et al. Differences in the association between sickness absence and long-term sub-optimal health

- by occupational position: a 14-year follow-up in the GAZEL cohort. *Occup Environ Med*. 2011 Oct;68(10):729-33.
19. Kivimäki M, Head J, Ferrie JE, al. e. Sickness absence as a global measure of health: evidence from mortality in the Whitehall II prospective cohort study. *BMJ*. 2003 Aug 16;327(7411):364.
 20. Hensing G. Swedish Council on Technology Assessment in Health Care (SBU). Chapter 4. Methodological aspects in sickness-absence research. *Scand J Public Health Suppl*. 2004;63:44-8.
 21. Voss M, Stark S, Alfredsson L, Vingard E, Josephson M. Comparisons of self-reported and register data on sickness absence among public employees in Sweden. *Occup Environ Med*. 2008 Jan;65(1):61-7.
 22. Hensing G, Alexanderson K, Allebeck P, Bjurulf P. How to measure sickness absence? Literature review and suggestion of five basic measures. *Scand J Soc Med*. 1998 Jun;26(2):133-44.
 23. Borg K, Goine H, Soderberg E, Marnetoft SU, Alexanderson K. Comparison of seven measures of sickness absence based on data from three counties in Sweden. *Work*. 2006;26(4):421-8.
 24. Hensing G. The measurements of sickness absence—a theoretical perspective. *Norsk Epidemiologi*. 2009;19(2):147-51.
 25. Hensing G, Alexanderson K, Allebeck P, Bjurulf P. Sick-leave due to psychiatric disorder: higher incidence among women and longer duration for men. *Br J Psychiatry*. 1996 Dec;169(6):740-6.
 26. Alexanderson K. A structure for categorisation of studies of sickness absence/disability pension. Division of Insurance Medicine, Karolinska Institutet;2015.
 27. Försäkringsmedicinska beslutsstödet. En långtidsuppföljning av förändringar i sjukskrivningsmönster. (Decision support in insurance medical. A long-term follow-up of changes in sick-leave patterns) (In Swedish). Socialförsäkringsrapport (Social Insurance Report) 2011:7, Social Insurance Agency 2011.
 28. Skaner Y, Nilsson GH, Arrelöv B, Lindholm C, Hinas E, Wilteus AL, et al. Use and usefulness of guidelines for sickness certification: results from a national survey of all general practitioners in Sweden. *BMJ Open*. 2011;1(2):e000303.
 29. En utvärdering av sjukskrivningsprocessen efter införandet av de nya sjukförsäkringsreglerna 2008-07-01. (An evaluation of the sick-leave process after the introduction of the new social insurance rules 2008-07-01) (In Swedish). Socialförsäkringsrapport (Social Insurance Report) 2011:15, Social Insurance Agency 2011.
 30. OECD. Sickness, disability and work: breaking the barriers: a synthesis of findings across OECD countries. Paris: OECD Publishing. 2010.
 31. Lidwall U. Termination of sickness benefits or transition to disability pension after changes in sickness insurance: a Swedish register study. *Disabil Rehabil*. 2013 Jan;35(2):118-24.
 32. Thorsen SV, Friberg C, Lundstrom B, Kausto J, Örnelius K, Sundell T, et al. Sickness absence in the Nordic countries. Copenhagen: Nordic Social Statistical Committee. 2015.
 33. www.fk.se.
 34. Analyzing the variation in the level of sickness absence-Essential explanations to the ups and downs of sick leave. Social Insurance Report 2014:17, Social Insurance Agency 2014.
 35. Långtidssjukskrivna (Long-term sickness absentees) (In Swedish). Socialförsäkringsrapport (Social Insurance Report) 2010:16, Social Insurance Agency 2010.
 36. Sjukfrånvaro i psykiska diagnoser. En studie av Sveriges befolkning 16–64 år. (Sick leave in psychiatric diagnoses. A study of the Swedish population aged 16-64) (In Swedish)

- Socialförsäkringsrapport (Social Insurance Report) 2014:4, Social Insurance Agency. 2014.
37. Allebeck P, Mastekaasa A. Swedish Council on Technology Assessment in Health Care (SBU). Chapter 5. Risk factors for sick leave - general studies. *Scand J Public Health Suppl.* 2004;63:49-108.
 38. Laaksonen M, Mastekaasa A, Martikainen P, Rahkonen O, Piha K, Lahelma E. Gender differences in sickness absence--the contribution of occupation and workplace. *Scand J Work Environ Health.* 2010 Sep;36(5):394-403.
 39. Mastekaasa A. Sickness absence in female- and male-dominated occupations and workplaces. *Soc Sci Med.* 2005 May;60(10):2261-72.
 40. Eshoj P, Jepsen JR, Nielsen CV. Long-term sickness absence - risk indicators among occupationally active residents of a Danish county. *Occup Med (Lond).* 2001 Aug;51(5):347-53.
 41. Sumanen H, Pietilainen O, Lahti J, Lahelma E, Rahkonen O. Interrelationships between education, occupational class and income as determinants of sickness absence among young employees in 2002-2007 and 2008-2013. *BMC Public Health.* 2015;15:332.
 42. Lallukka T, Lahelma E, Rahkonen O. Changes in economic difficulties and subsequent sickness absence: a prospective register-linkage study. *BMJ Open.* 2013;3(1).
 43. Duijts SF, Kant I, Swaen GM, van den Brandt PA, Zeegers MP. A meta-analysis of observational studies identifies predictors of sickness absence. *J Clin Epidemiol.* 2007 Nov;60(11):1105-15.
 44. Vistnes J. Gender differences in days lost from work due to illness. *Ind Labor Relat Rev.* 1997;50(2):304-23.
 45. Ropponen A, Alexanderson K, Svedberg P. Part-time work or social benefits as predictors for disability pension: a prospective study of Swedish twins. *Int J Behav Med.* 2014 Apr;21(2):329-36.
 46. Akhavan S, Bildt CO, Franzen EC, Wamala S. Health in relation to unemployment and sick leave among immigrants in Sweden from a gender perspective. *J Immigr Health.* 2004 Jul;6(3):103-18.
 47. Floderus B, Hagman M, Aronsson G, Marklund S, Wikman A. Medically certified sickness absence with insurance benefits in women with and without children. *Eur J Public Health.* 2012 Feb;22(1):85-92.
 48. Andrea H, Beurskens AJ, Metsemakers JF, van Amelsvoort LG, van den Brandt PA, van Schayck CP. Health problems and psychosocial work environment as predictors of long term sickness absence in employees who visited the occupational physician and/or general practitioner in relation to work: a prospective study. *Occup Environ Med.* 2003 Apr;60(4):295-300.
 49. Duijts SF, Kant IJ, Landeweerd JA, Swaen GM. Prediction of sickness absence: development of a screening instrument. *Occup Environ Med.* 2006 Aug;63(8):564-9.
 50. Knudsen AK, Harvey SB, Mykletun A, Overland S. Common mental disorders and long-term sickness absence in a general working population. The Hordaland Health Study. *Acta Psychiatr Scand.* 2013 Apr;127(4):287-97.
 51. Borritz M, Christensen KB, Bultmann U, Rugulies R, Lund T, Andersen I, et al. Impact of burnout and psychosocial work characteristics on future long-term sickness absence. Prospective results of the Danish PUMA Study among human service workers. *J Occup Environ Med.* 2010 Oct;52(10):964-70.
 52. Roelen CA, Bultmann U, Groothoff J, van Rhenen W, Mageroy N, Moen BE, et al. Physical and mental fatigue as predictors of sickness absence among Norwegian nurses. *Res Nurs Health.* 2013 Oct;36(5):453-65.
 53. Stansfeld S, Candy B. Psychosocial work environment and mental health--a meta-analytic review. *Scand J Work Environ Health.* 2006 Dec;32(6):443-62.

54. Akerstedt T, Kecklund G, Alfredsson L, Selen J. Predicting long-term sickness absence from sleep and fatigue. *J Sleep Res.* 2007 Dec;16(4):341-5.
55. Janssen N, Kant IJ, Swaen GM, Janssen PP, Schroer CA. Fatigue as a predictor of sickness absence: results from the Maastricht cohort study on fatigue at work. *Occup Environ Med.* 2003 Jun;60 Suppl 1:i71-6.
56. Kaaria S, Laaksonen M, Leino-Arjas P, Saastamoinen P, Lahelma E. Low back pain and neck pain as predictors of sickness absence among municipal employees. *Scand J Public Health.* 2012 Mar;40(2):150-6.
57. Korpela K, Roos E, Lallukka T, Rahkonen O, Lahelma E, Laaksonen M. Different measures of body weight as predictors of sickness absence. *Scand J Public Health.* 2013 Feb;41(1):25-31.
58. Kivimäki M, Sutinen R, Elovainio M, Vahtera J, Rasanen K, Toyry S, et al. Sickness absence in hospital physicians: 2 year follow up study on determinants. *Occup Environ Med.* 2001 Jun;58(6):361-6.
59. Salonsalmi A, Rahkonen O, Lahelma E, Laaksonen M. Changes in alcohol drinking and subsequent sickness absence. *Scand J Public Health.* 2015 Jun;43(4):364-72.
60. OECD. Mental Health and Work: Sweden.2013.
61. WHO. Mental Health and Work: Impact, Issues and Good Practices. Geneva: World Health Organization2000.
62. Widanarko B, Legg S, Devereux J, Stevenson M. Interaction between physical and psychosocial risk factors on the presence of neck/shoulder symptoms and its consequences. *Ergonomics.* 2015 Sep;58(9):1507-18.
63. Lesuffleur T, Chastang JF, Sandret N, Niedhammer I. Psychosocial factors at work and sickness absence: results from the French national SUMER survey. *Am J Ind Med.* 2014 Jun;57(6):695-708.
64. Kivimäki M, Vahtera J, Kawachi I, Ferrie JE, Oksanen T, Joensuu M, et al. Psychosocial work environment as a risk factor for absence with a psychiatric diagnosis: an instrumental-variables analysis. *Am J Epidemiol.* 2010 Jul 15;172(2):167-72.
65. Karasek R, Brisson C, Kawakami N, Houtman I, Bongers P, Amick B. The Job Content Questionnaire (JCQ): an instrument for internationally comparative assessments of psychosocial job characteristics. *J Occup Health Psychol.* 1998 Oct;3(4):322-55.
66. Mather L, Bergstrom G, Blom V, Svedberg P. High Job Demands, Job Strain, and Iso-Strain Are Risk Factors for Sick Leave due to Mental Disorders: A Prospective Swedish Twin Study With a 5-Year Follow-Up. *J Occup Environ Med.* 2015 Aug;57(8):858-65.
67. WHO. Mental health : new understanding, new hope. The World health report : 2001.
68. WHO. Health topics: Mental health. 2012 [cited 2015 06-20]; Available from: http://www.who.int/topics/mental_health/en.
69. APA. Diagnostic and Statistical Manual of Mental Disorders DSM-V Fifth Edition. 5th ed. 2013.
70. WHO. The ICD-10 Classification of Mental and Behavioural Disorders. 2013 [cited 2015 09-30]; Available from: <http://www.who.int/classifications/icd/en/bluebook.pdf>.
71. Rahman S, Alexanderson K, Jokinen J, Mittendorfer-Rutz E. Risk factors for suicidal behaviour in individuals on disability pension due to common mental disorders - a nationwide register-based prospective cohort study in Sweden. *PLoS One.* 2014;9(5):e98497.
72. Adler DA, McLaughlin TJ, Rogers WH, Chang H, Lapitsky L, Lerner D. Job performance deficits due to depression. *Am J Psychiatry.* 2006 Sep;163(9):1569-76.
73. Goldberg DP, Huxley P. Common mental disorders a bio-social model. London: Tavistock/Routledge;1992.
74. Batterham PJ, Christensen H, Calear AL. Anxiety symptoms as precursors of major depression and suicidal ideation. *Depress Anxiety.* 2013 Mar 14.

75. Lu D, Andersson TM, Fall K, Hultman CM, Czene K, Valdimarsdottir U, et al. Increased risk for psychiatric disorders immediately before and after cancer diagnosis: A nationwide matched cohort study in Sweden. *Psychoneuroendocrinology*. 2015 Nov;61:50.
76. Bjorkenstam E, Ljung R, Burstrom B, Mittendorfer-Rutz E, Hallqvist J, Weitoft GR. Quality of medical care and excess mortality in psychiatric patients--a nationwide register-based study in Sweden. *BMJ Open*. 2012;2:e000778.
77. Dorner TE, Alexanderson K, Svedberg P, Tinghog P, Ropponen A, Mittendorfer-Rutz E. Synergistic effect between back pain and common mental disorders and the risk of future disability pension: a nationwide study from Sweden. *Psychol Med*. 2015 Oct 15:1-12.
78. Cafferata GL, Meyers SM. Pathways to psychotropic drugs. Understanding the basis of gender differences. *Med Care*. 1990 Apr;28(4):285-300.
79. Kessler RC, Amminger GP, Aguilar-Gaxiola S, Alonso J, Lee S, Ustun TB. Age of onset of mental disorders: a review of recent literature. *Curr Opin Psychiatry*. 2007 Jul;20(4):359-64.
80. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005 Jun;62(6):593-602.
81. WHO. Preventing suicide. A global imperative. World Health Organization 2014.
82. WHO. Age standardized suicide rates. 2012 [cited 2015 08-17]; Available from: http://www.who.int/gho/mental_health/suicide_rates/en/.
83. Hawton K, van Heeringen K. Suicide. *Lancet*. 2009 Apr 18;373(9672):1372-81.
84. Dödsorsaksregistret (The Cause of Death Register) (In Swedish). Stockholm, Sweden. 2015 [cited 2015 10-19]; Available from: www.socialstyrelsen.se.
85. Skegg K. Self-harm. *Lancet*. 2005 Oct 22-28;366(9495):1471-83.
86. Hawton K, Van Heeringen K. Introduction. In: Hawton K, Van Heeringen K, editors. *The International Handbook of suicide and attempted suicide*. Chichester: John Wiley & Sons; 2000.
87. Hawton K, Harriss L, Hall S, Simkin S, Bale E, Bond A. Deliberate self-harm in Oxford, 1990-2000: a time of change in patient characteristics. *Psychol Med*. 2003 Aug;33(6):987-95.
88. Schmidtke A, Bille-Brahe U, DeLeo D, Kerkhof A, Bjerke T, Crepet P, et al. Attempted suicide in Europe: rates, trends and sociodemographic characteristics of suicide attempters during the period 1989-1992. Results of the WHO/EURO Multicentre Study on Parasuicide. *Acta Psychiatr Scand*. 1996 May;93(5):327-38.
89. Douglas J, Cooper J, Amos T, Webb R, Guthrie E, Appleby L. "Near-fatal" deliberate self-harm: characteristics, prevention and implications for the prevention of suicide. *J Affect Disord*. 2004 Apr;79(1-3):263-8.
90. Patientregistret. (National Patient Register) (In Swedish). Stockholm. Socialstyrelsen (National Board of Health and Welfare); 2015 [cited 2015 04-13]; Available from: <http://www.socialstyrelsen.se>.
91. Krug G, E., Dahlberg L, L., Mercy J, A., Zwi AB, Lozano R. *World Report on Health and Violence*. Geneva: World Health Organization; 2002.
92. Linsley KR, Schapira K, Kelly TP. Open verdict v. suicide - importance to research. *Br J Psychiatry*. 2001 May;178:465-8.
93. Mittendorfer-Rutz E, Rasmussen F, Wasserman D. Restricted fetal growth and adverse maternal psychosocial and socioeconomic conditions as risk factors for suicidal behaviour of offspring: a cohort study. *Lancet*. 2004 Sep 25-Oct 1;364(9440):1135-40.
94. Kosidou K, Magnusson C, Mittendorfer-Rutz E, Hallqvist J, Hellner Gumpert C, Idrizbegovic S, et al. Recent time trends in levels of self-reported anxiety, mental health service use and suicidal behaviour in Stockholm. *Acta Psychiatr Scand*. 2010 Jul;122(1):47-55.

95. Tidemalm D, Langstrom N, Lichtenstein P, Runeson B. Risk of suicide after suicide attempt according to coexisting psychiatric disorder: Swedish cohort study with long term follow-up. *BMJ*. 2008;337:a2205.
96. Kessler RC, Borges G, Walters EE. Prevalence of and risk factors for lifetime suicide attempts in the National Comorbidity Survey. *Arch Gen Psychiatry*. 1999 Jul;56(7):617-26.
97. Hepple J, Quinton C. One hundred cases of attempted suicide in the elderly. *Br J Psychiatry*. 1997 Jul;171:42-6.
98. Petronis KR, Samuels JF, Moscicki EK, Anthony JC. An epidemiologic investigation of potential risk factors for suicide attempts. *Soc Psychiatry Psychiatr Epidemiol*. 1990 Jul;25(4):193-9.
99. Petronis KR, Samuels JF, Moscicki EK, Anthony JC. Suicidal behaviour and the labour market. In: Hawton K, Van Heeringen K, editors. *Handbook of suicide and attempted suicide*. Chichester: John Wiley & Sons; 2000.
100. Taylor R, Page A, Morrell S, Carter G, Harrison J. Socio-economic differentials in mental disorders and suicide attempts in Australia. *Br J Psychiatry*. 2004 Dec;185:486-93.
101. Beautrais AL. Risk factors for suicide and attempted suicide among young people. *Aust N Z J Psychiatry*. 2000 Jun;34(3):420-36.
102. Nordentoft M, Mortensen PB, Pedersen CB. Absolute risk of suicide after first hospital contact in mental disorder. *Arch Gen Psychiatry*. 2011 Oct;68(10):1058-64.
103. Haw C, Hawton K, Houston K, Townsend E. Psychiatric and personality disorders in deliberate self-harm patients. *Br J Psychiatry*. 2001 Jan;178(1):48-54.
104. Runeson B, Haglund A, Lichtenstein P, Tidemalm D. Suicide risk after nonfatal self-harm: a national cohort study, 2000-2008. *J Clin Psychiatry*. 2015 Aug 4.
105. Cavanagh JT, Carson AJ, Sharpe M, Lawrie SM. Psychological autopsy studies of suicide: a systematic review. *Psychol Med*. 2003 Apr;33(3):395-405.
106. Isometsa ET, Aro HM, Henriksson MM, Heikkinen ME, Lonnqvist JK. Suicide in major depression in different treatment settings. *J Clin Psychiatry*. 1994 Dec;55(12):523-7.
107. Riihimaki K, Vuorilehto M, Melartin T, Haukka J, Isometsa E. Incidence and predictors of suicide attempts among primary-care patients with depressive disorders: a 5-year prospective study. *Psychol Med*. 2013 Apr 10:1-12.
108. Blair-West GW, Mellsop GW, Eyeson-Annan ML. Down-rating lifetime suicide risk in major depression. *Acta Psychiatr Scand*. 1997 Mar;95(3):259-63.
109. Inskip HM, Harris EC, Barraclough B. Lifetime risk of suicide for affective disorder, alcoholism and schizophrenia. *Br J Psychiatry*. 1998 Jan;172:35-7.
110. Harris EC, Barraclough B. Excess mortality of mental disorder. *Br J Psychiatry*. 1998 Jul;173:11-53.
111. McGirr A, Renaud J, Bureau A, Seguin M, Lesage A, Turecki G. Impulsive-aggressive behaviours and completed suicide across the life cycle: a predisposition for younger age of suicide. *Psychol Med*. 2008 Mar;38(3):407-17.
112. Owens D, Horrocks J, House A. Fatal and non-fatal repetition of self-harm. Systematic review. *Br J Psychiatry*. 2002 Sep;181:193-9.
113. Harris EC, Barraclough B. Suicide as an outcome for mental disorders. A meta-analysis. *Br J Psychiatry*. 1997 Mar;170:205-28.
114. Hawton K, Zahl D, Weatherall R. Suicide following deliberate self-harm: long-term follow-up of patients who presented to a general hospital. *Br J Psychiatry*. 2003 Jun;182:537-42.
115. Zahl DL, Hawton K. Repetition of deliberate self-harm and subsequent suicide risk: long-term follow-up study of 11,583 patients. *Br J Psychiatry*. 2004 Jul;185:70-5.
116. Suominen K, Isometsa E, Ostamo A, Lonnqvist J. Level of suicidal intent predicts overall mortality and suicide after attempted suicide: a 12-year follow-up study. *BMC Psychiatry*. 2004 Apr 20;4:11.

117. Cooper J, Kapur N, Webb R, Lawlor M, Guthrie E, Mackway-Jones K, et al. Suicide after deliberate self-harm: a 4-year cohort study. *Am J Psychiatry*. 2005 Feb;162(2):297-303.
118. Harris EC, Barraclough BM. Suicide as an outcome for medical disorders. *Medicine (Baltimore)*. 1994 Nov;73(6):281-96.
119. Stenager E, Stenager E. Physical illness and suicidal behaviour. In: Hawton K, van Heeringen K, editors. *The international Handbook of suicide and attempted suicide*. West Sussex, England Wiley & Sons Ltd.; 2000. p. 405-20.
120. Hawton K, Fagg J, Marsack P. Association between epilepsy and attempted suicide. *J Neurol Neurosurg Psychiatry*. 1980 Feb;43(2):168-70.
121. Webb RT, Lichtenstein P, Dahlin M, Kapur N, Ludvigsson JF, Runeson B. Unnatural deaths in a national cohort of people diagnosed with diabetes. *Diabetes Care*. 2014 Aug;37(8):2276-83.
122. Gala C, Pergami A, Catalan J, Riccio M, Durbano F, Musicco M, et al. Risk of deliberate self-harm and factors associated with suicidal behaviour among asymptomatic individuals with human immunodeficiency virus infection. *Acta Psychiatr Scand*. 1992 Jul;86(1):70-5.
123. Mann JJ, Waternaux C, Haas GL, Malone KM. Toward a clinical model of suicidal behavior in psychiatric patients. *Am J Psychiatry*. 1999 Feb;156(2):181-9.
124. De Leo D, Scocco P, Marietta P, Schmidtke A, Bille-Brahe U, Kerkhof AJ, et al. Physical illness and parasuicide: evidence from the European Parasuicide Study Interview Schedule (EPSIS/WHO-EURO). *Int J Psychiatry Med*. 1999;29(2):149-63.
125. Qin P, Agerbo E, Mortensen PB. Suicide risk in relation to socioeconomic, demographic, psychiatric, and familial factors: a national register-based study of all suicides in Denmark, 1981-1997. *Am J Psychiatry*. 2003 Apr;160(4):765-72.
126. Mittendorfer-Rutz E, Rasmussen F, Wasserman D. Familial clustering of suicidal behaviour and psychopathology in young suicide attempters. A register-based nested case control study. *Soc Psychiatry Psychiatr Epidemiol*. 2008 Jan;43(1):28-36.
127. Johnson JG, Cohen P, Gould MS, Kasen S, Brown J, Brook JS. Childhood adversities, interpersonal difficulties, and risk for suicide attempts during late adolescence and early adulthood. *Arch Gen Psychiatry*. 2002 Aug;59(8):741-9.
128. Martiniuk AL, Chen HY, Glozier N, Patton G, Senserrick T, Williamson A, et al. High alcohol use a strong and significant risk factor for repetitive self-harm in female and male youth: a prospective cohort study. *Am J Drug Alcohol Abuse*. 2015 Sep;41(5):465-73.
129. Dragisic T, Dickov A, Dickov V, Mijatovic V. Drug Addiction as Risk for Suicide Attempts. *Mater Sociomed*. 2015 Jun;27(3):188-91.
130. Eagles JM, Carson DP, Begg A, Naji SA. Suicide prevention: a study of patients' views. *Br J Psychiatry*. 2003 Mar;182:261-5.
131. Beautrais AL, Joyce PR, Mulder RT. Precipitating factors and life events in serious suicide attempts among youths aged 13 through 24 years. *J Am Acad Child Adolesc Psychiatry*. 1997 Nov;36(11):1543-51.
132. Gjesdal S, Bratberg E. Diagnosis and duration of sickness absence as predictors for disability pension: results from a three-year, multi-register based and prospective study. *Scand J Public Health*. 2003;31(4):246-54.
133. Gjesdal S, Ringdal PR, Haug K, Maeland JG. Predictors of disability pension in long-term sickness absence: results from a population-based and prospective study in Norway 1994-1999. *Eur J Public Health*. 2004 Dec;14(4):398-405.
134. Borg K, Hensing G, Alexanderson K. Risk factors for disability pension over 11 years in a cohort of young persons initially sick-listed with low back, neck, or shoulder diagnoses. *Scand J Public Health*. 2004;32(4):272-8.

135. Labriola M, Lund T. Self-reported sickness absence as a risk marker of future disability pension. Prospective findings from the DWECS/DREAM study 1990-2004. *Int J Med Sci*. 2007;4(3):153-8.
136. Karlsson NE, Carstensen JM, Gjesdal S, Alexanderson KA. Risk factors for disability pension in a population-based cohort of men and women on long-term sick leave in Sweden. *Eur J Public Health*. 2008 Jun;18(3):224-31.
137. Ishtiak-Ahmed K, Perski A, Mittendorfer-Rutz E. Risk markers of all-cause and diagnosis-specific disability pension--a prospective cohort study of individuals sickness absent due to stress-related mental disorders. *BMC Public Health*. 2014;14:805.
138. Kivimaki M, Ferrie JE, Hagberg J, Head J, Westerlund H, Vahtera J, et al. Diagnosis-specific sick leave as a risk marker for disability pension in a Swedish population. *J Epidemiol Community Health*. 2007 Oct;61(10):915-20.
139. Gjesdal S, Ringdal PR, Haug K, Maeland JG. Long-term sickness absence and disability pension with psychiatric diagnoses: a population-based cohort study. *Nord J Psychiatry*. 2008;62(4):294-301.
140. Bratberg E, Gjesdal S, Maeland JG. Sickness absence with psychiatric diagnoses: Individual and contextual predictors of permanent disability. *Health Place*. 2009 Mar;15(1):308-14.
141. Friberg E, Jansson C, Mittendorfer-Rutz E, Rosenhall U, Alexanderson K. Sickness absence due to otoaudiological diagnoses and risk of disability pension: a nationwide Swedish prospective cohort study. *PLoS One*. 2012;7(1):e29966.
142. Kausto J, Virta L, Luukkonen R, Viikari-Juntura E. Associations between partial sickness benefit and disability pensions: initial findings of a Finnish nationwide register study. *BMC Public Health*. 2010;10:361.
143. Kausto J, Solovieva S, Virta LJ, Viikari-Juntura E. Partial sick leave associated with disability pension: propensity score approach in a register-based cohort study. *BMJ Open*. 2012;2(6).
144. Gjesdal S, Bratberg E, Maeland JG. Gender differences in disability after sickness absence with musculoskeletal disorders: five-year prospective study of 37,942 women and 26,307 men. *BMC Musculoskelet Disord*. 2011;12:37.
145. Vaez M, Rylander G, Nygren A, Asberg M, Alexanderson K. Sickness absence and disability pension in a cohort of employees initially on long-term sick leave due to psychiatric disorders in Sweden. *Soc Psychiatry Psychiatr Epidemiol*. 2007 May;42(5):381-8.
146. Mittendorfer-Rutz E, Harkanen T, Tiihonen J, Haukka J. Association of socio-demographic factors, sick-leave and health care patterns with the risk of being granted a disability pension among psychiatric outpatients with depression. *PLoS One*. 2014;9(6):e99869.
147. Wedegaertner F, Arnhold-Kerri S, Sittaro NA, Bleich S, Geyer S, Lee WE. Depression- and anxiety-related sick leave and the risk of permanent disability and mortality in the working population in Germany: a cohort study. *BMC Public Health*. 2013;13:145.
148. Gjesdal S, Ringdal PR, Haug K, al. e. Mortality after long-term sickness absence: prospective cohort study. *Eur J Public Health*. 2008 Oct;18(5):517-21.
149. Bjorkenstam E, Weitoft GR, Lindholm C, Bjorkenstam C, Alexanderson K, Mittendorfer-Rutz E. Associations between number of sick-leave days and future all-cause and cause-specific mortality: a population-based cohort study. *BMC Public Health*. 2014;14:733.
150. Singh-Manoux A, Gueguen A, Ferrie J, Shipley M, Martikainen P, Bonenfant S, et al. Gender differences in the association between morbidity and mortality among middle-aged men and women. *Am J Public Health*. 2008 Dec;98(12):2251-7.

151. Kivimaki M, Head J, Ferrie JE, Singh-Manoux A, Westerlund H, Vahtera J, et al. Sickness absence as a prognostic marker for common chronic conditions: analysis of mortality in the GAZEL study. *Occup Environ Med*. 2008 Dec;65(12):820-6.
152. Jansson C, Mittendorfer-Rutz E, Alexanderson K. Sickness absence because of musculoskeletal diagnoses and risk of all-cause and cause-specific mortality: a nationwide Swedish cohort study. *Pain*. 2012;153(5):998-1005.
153. Bryngelson A, Asberg M, Nygren A, Jensen I, Mittendorfer-Rutz E. All-Cause and Cause-Specific Mortality after Long-Term Sickness Absence for Psychiatric Disorders: A Prospective Cohort Study. *PLoS One*. 2013;8(6):e67887.
154. Qin P, Agerbo E, Westergaard-Nielsen N, Eriksson T, Mortensen PB. Gender differences in risk factors for suicide in Denmark. *Br J Psychiatry*. 2000 Dec;177:546-50.
155. Lemogne C, Nabi H, Melchior M, Goldberg M, Limosin F, Consoli SM, et al. Mortality associated with depression as compared with other severe mental disorders: a 20-year follow-up study of the GAZEL cohort. *J Psychiatr Res*. 2013 Jul;47(7):851-7.
156. Gustafsson K, Marklund S. Consequences of sickness presence and sickness absence on health and work ability: a Swedish prospective cohort study. *Int J Occup Med Environ Health*. 2011 Jun;24(2):153-65.
157. Kivimaki M, Ferrie JE, Shipley MJ, Vahtera J, Singh-Manoux A, Marmot MG, et al. Low medically certified sickness absence among employees with poor health status predicts future health improvement: the Whitehall II study. *Occup Environ Med*. 2008 Mar;65(3):208-10.
158. Koopmans PC, Bultmann U, Roelen CA, Hoedeman R, van der Klink JJ, Groothoff JW. Recurrence of sickness absence due to common mental disorders. *Int Arch Occup Environ Health*. 2011 Feb;84(2):193-201.
159. Roelen CA, Koopmans PC, Anema JR, van der Beek AJ. Recurrence of medically certified sickness absence according to diagnosis: a sickness absence register study. *J Occup Rehabil*. 2010 Mar;20(1):113-21.
160. Roelen CA, Koopmans PC, Schreuder JA, Anema JR, van der Beek AJ. The history of registered sickness absence predicts future sickness absence. *Occup Med (Lond)*. 2011 Mar;61(2):96-101.
161. Virtanen M, Kivimaki M, Vahtera J, Elovainio M, Sund R, Virtanen P, et al. Sickness absence as a risk factor for job termination, unemployment, and disability pension among temporary and permanent employees. *Occup Environ Med*. 2006 Mar;63(3):212-7.
162. Wikman A, Wiberg M, Marklund S, Alexanderson K. Activities and sources of income after a period of long-term sick leave--a population-based prospective cohort study. *BMC Public Health*. 2012;12:745.
163. Wiberg M, Friberg E, Palmer E, Stenbeck M. Sickness absence and subsequent disposable income: A population-based cohort study. *Scand J Public Health*. 2015 Mar 27.
164. Ludvigsson JF, Otterblad-Olausson P, Pettersson BU, Ekbom A. The Swedish personal identity number: possibilities and pitfalls in healthcare and medical research. *Eur J Epidemiol*. 2009;24(11):659-67.
165. Longitudinell integrationsdatabas för Sjukförsäkrings- och Arbetsmarknadsstudier (LISA) 1990–2009. (Longitudinal Integration Database for Health Insurance and Labour Market Studies (LISA) 1990-2009.) (In Swedish). Statistiska centralbyrån (Statistics Sweden); 2011 [cited 2015 06-05]; Available from: www.scb.se.
166. MiDAS: Sjukpenning och Rehabiliteringspenning. (MiDAS: Sickness benefit and Rehabilitation benefit.) (In Swedish). Försäkringskassan (Social Insurance Agency); 2011 [cited 2015 05-30]; Available from: www.forsakringskassan.se.
167. Forsberg L, Rydh H, Björkenstam E, Jacobsson A, Nyqvist K, Heurgren M. Kvalitet och innehåll i patientregistret. Utskrivningar från slutenvården 1964–2007 och besök i specialiserad öppenvård (exklusive primärvårdsbesök) 1997–2007. (Quality and content of the Patient Register. Discharges from inpatient care in 1964-2007 and visits to specialised

- outpatient care (excluding primary care visits) in 1997-2007.) (In Swedish): Socialstyrelsen.2009.
168. Wettermark B, Hammar N, Fored CM, Leimanis A, Otterblad Olausson P, Bergman U, et al. The new Swedish Prescribed Drug Register--opportunities for pharmacoepidemiological research and experience from the first six months. *Pharmacoepidemiol Drug Saf.* 2007 Jul;16(7):726-35.
 169. Guidelines for ATC classification and DDD assignment. WHO Collaborating Centre for Drug Statistics Methodology. Oslo: World Health Organization (WHO); 2005 [cited 2015 08-20]; Available from: www.whocc.no.
 170. Regionala indelningar i Sverige den 1 januari 2003. Del 1 (Regional divisions in Sweden on 1 January 2003. Part 1) (In Swedish). Statistics Sweden.2003.
 171. Jones B, Nagin D, Roeder K. A SAS Procedure Based on Mixture Models for Estimating Developmental Trajectories. *Sociological Methods & Research* 2001;29(3):374-93.
 172. Burns BJ, Ryan Wagner H, Gaynes BN, Wells KB, Schulberg HC. General medical and specialty mental health service use for major depression. *Int J Psychiatry Med.* 2000;30(2):127-43.
 173. Angst J, Gamma A, Gastpar M, Lepine JP, Mendlewicz J, Tylee A. Gender differences in depression. Epidemiological findings from the European DEPRES I and II studies. *Eur Arch Psychiatry Clin Neurosci.* 2002 Oct;252(5):201-9.
 174. Rutz W, von Knorring L, Pihlgren H, Rihmer Z, Walinder J. Prevention of male suicides: lessons from Gotland study. *Lancet.* 1995 Feb 25;345(8948):524.
 175. Hakko H, Manninen J, Karvonen K, Särkioja T, Meyer-Rochow VB, Räsänen P, et al. Association between physical illnesses and depressive symptoms requiring hospitalization in suicide victims. *Psychiatry Research.* 2008;160:271-7.
 176. Cherpitel CJ, Ye Y, Bond J. Attributable risk of injury associated with alcohol use: cross-national data from the emergency room collaborative alcohol analysis project. *Am J Public Health.* 2005 Feb; 95(2):266-72.
 177. Leone SS. A disabling combination: fatigue and depression. *Br J Psychiatry.* 2010 Aug; 197(2):86-7.
 178. Ishtiak-Ahmed K, Perski A, Mittendorfer-Rutz E. Predictors of suicidal behaviour in 36,304 individuals sickness absent due to stress-related mental disorders -- a Swedish register linkage cohort study. *BMC Public Health.* 2013;13:492.
 179. Björkenstam C, Alexanderson K, Wiberg M, Hillert J, Tinghög P. Heterogeneity of sickness absence and disability pension trajectories among individuals with MS. *Multiple Sclerosis Journal-Experimental, Translational and Clinical.* 2015;DOI: 10.1177/2055217315595638:1-11.
 180. Virtanen M, Kivimäki M, Zins M, Dray-Spira R, Oksanen T, Ferrie JE, et al. Lifestyle-related risk factors and trajectories of work disability over 5 years in employees with diabetes: findings from two prospective cohort studies. *Diabet Med.* 2015 Apr 27.
 181. Stansfeld S, Feeney A, Head J, Canner R, North F, Marmot M. Sickness absence for psychiatric illness: the Whitehall II Study. *Soc Sci Med.* 1995 Jan;40(2):189-97.
 182. Hawton K, Casanas ICC, Haw C, Saunders K. Risk factors for suicide in individuals with depression: a systematic review. *J Affect Disord.* 2013 May;147(1-3):17-28.
 183. Holma KM, Melartin TK, Haukka J, Holma IA, Sokero TP, Isometsä ET. Incidence and predictors of suicide attempts in DSM-IV major depressive disorder: a five-year prospective study. *Am J Psychiatry.* 2010 Jul;167(7):801-8.
 184. Runeson BS, Beskow J, Waern M. The suicidal process in suicides among young people. *Acta Psychiatr Scand.* 1996 Jan; 93(1):35-42.
 185. Wasserman D, Rihmer Z, Rujescu D, Sarchiapone M, Sokolowski M, Titelman D, et al. The European Psychiatric Association (EPA) guidance on suicide treatment and prevention. *Eur Psychiatry.* 2012 Feb;27(2):129-41.

186. Zimmerman M, McDermt W, Mattia JI. Frequency of anxiety disorders in psychiatric outpatients with major depressive disorder. *Am J Psychiatry*. 2000 Aug;157(8):1337-40.
187. Rothman K, Greenland S, Lash TL. *Modern Epidemiology*. 3rd ed. Philadelphia:Lippincott Williams & Wilkins; 2008.
188. Ludvigsson JF, Andersson E, Ekbom A, Feychting M, Kim JL, Reuterwall C, et al. External review and validation of the Swedish national inpatient register. *BMC Public Health*. 2011;11:450.
189. Soderberg E, Alexanderson K. Sickness certificates as a basis for decisions regarding entitlement to sickness insurance benefits. *Scand J Public Health*. 2005;33(4):314-20.
190. Ljungdahl LO, Bjurulf P. The accordance of diagnoses in a computerized sick-leave register with doctor's certificates and medical records. *Scand J Soc Med*. 1991 Sep;19(3):148-53.
191. Shrivastava A, Johnston M, Bureau Y. Stigma of Mental Illness-1: Clinical reflections. *Mens Sana Monogr*. 2012 Jan;10(1):70-84.